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ABSTRACTS

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Effect of salt intake on P-glycoprotein expression induced by cyclosporine A in circulating lymphocytes in rats. *M. Andújar, C. Ramírez, E. Vergara, M. Gómez-Morales, A. Osuna, A. Olmo, F. Arrebola, M.J. García-Chicano, R.G. Del Moral, Department of Pathology, University Hospital, Nephrology Service, Virgen de las Nieves Hospital, Granada, Spain.* P-170 glycoprotein (P-gp) is a detoxicant system related with multidrug resistance (MDR) in some tumors. The protein removes from the cell hydrophobic substances such as chemotherapeutic and immunosuppressive agents, including cyclosporine A (CsA). Exposure of the renal parenchyma to therapeutic doses of CsA induces overexpression of P-gp in this tissue; this phenomenon is related with the presence of drug deposits. We developed a model of chronic CsA toxicity in Sprague-Dawley rats treated with 25 mg/kg/day CsA for 2 months and maintained on a standard diet or a sodium-free diet. We studied the percentage of cells positive for P-gp and mean channel fluorescence in circulating lymphocytes, using flow cytometry and indirect immunofluorescence (mAb JSB1, which recognizes P-gp). Positivity was detected in lymphocytes from all groups; however, the highest percentage; (61.3%; $P < 0.001$) and the highest mean channel fluorescence (15.3; $P < 0.05$) appeared in rats treated with CsA and fed the maintenance diet. Most groups of animals fed with the sodium-free diet had lower levels of P-gp expression and mean channel fluorescence in comparison with rats fed the maintenance diet. We conclude that CsA treatment and feeding with a maintenance (standard) diet induce a significant increase in P-gp expression in circulating lymphocytes in the rat. Our findings suggest a possible osmotic induction effect of diets with normal sodium content, and a potentially beneficial effect of restricted sodium intake in transplant patients receiving CsA treatment.

Citraturia and formation of calcium oxalate deposits in renal tissue following terminal ileon exclusion surgery: Experimental study. *J. Font, A. Gascón, E. Iglesias, R. Burdeus, J.M. Monge, A. Ingelmo, S. Urology and Nephrology, O. Polanco General Hospital, Teruel, Spain.* Partial ileal bypass (PIB) surgery has been used since 1963 as treatment for severe cases of hypercholesterolemia. The most frequent side effect of this type of surgery are diarrhea and nephrolithiasis. The entrance of acid and biliar salts to the colon produces in these patients hyperoxaluria. PIB patients appear to be at risk for kidney stone formation. The combination of reduced urinary volume and calcium oxalate precipitation inhibitor substance with increased calcium oxalate relative supersaturation produced an increase in nephrolithiasis risk. The aim of the present study is to evaluate the different renal byochemical alterations induced by this type of surgery in Wistar rats. We studied 70 Wistar rats aged 6 to 12 months. After feeding with a high cholesterol diet for six months, ten of them were sacrified and used as a control group. A group of 30 rats underwent terminal ileon resection. On another group of 30 rats terminal ileon by-pass was performed. After 30, 90 and 180 days, they were sacrified for histological study. Hyperoxaluria appeared in all the rats that underwent surgery. Calcium oxalate deposits in renal tissue were not found in any of the cases. The 24-hour urine citrate levels were normal. Diarrhea did not occur in any of the rats. Calcium and phosphor levels were not altered during the experience. In conclusion, hyperoxaluria resulting after terminal ileon exclusion surgery indicates the importance of acid and biliar salts as inductors of permeability in the colonic mucosa for oxalates. The absence of diarrhea justifies normocitraturia in our study and the later absence of calcium oxalate deposits in renal tissue.

Histological renal damage induced by hypercholesterolemic diet in Wistar rats: influence of terminal ileon exclusion surgery. *J. Font, A. Gascón, E. Iglesias, R. Burdeus, A. Yagüe, A. Ingelmo, S. Urology and Nephrology, O. Polanco General Hospital, Teruel, Spain.* Experimental investigations have suggested an important role for abnormal lipid metabolism as a factor in modulating progressive renal disease. Partial ileal bypass (PIB) surgery has been used since 1963 as treatment for severe cases of hypercholesterolemia. The most frequent side effect of this type of surgery are diarrhea and nephrolithiasis. However, there are no experimental studies about the effects of PIB surgery on renal histology. The present study examined the histological alterations in renal tissue induced by a high cholesterol diet. These are also compared with those found when cholesterol levels are normalized in plasma by PIB surgery. We studied 70 Wistar rats aged 6 to 12 months after feeding them a high cholesterol diet for six months. Ten of them were sacrified and used as a control group. The remaining 60 rats underwent terminal ileon exclusion surgery (resection or bypass), bringing their cholesterol to normal levels. After 30, 90 and 180 days, they were sacrified for histological study. The high cholesterol diet induced high cholesterol levels in plasma (68 ± 9 vs. 119 ± 14 mg/dl, $P < 0.05$). After terminal ileon exclusion surgery all the rats experimented an important decrease of plasma cholesterol, ranging from 15 to 48%. Renal injury consisted in tubulointerstitial injury in 8 cases, without signs of glomerulosclerosis. These findings were focal and bilateral, and did not depend on the type of surgery. In 14% of the rats we found lipid infiltration of the abdominal aorta. The control group presented the same renal damage identical in proportion and intensity. In conclusion, we found very low histological renal injury, basically consisting in tubulointerstitial nephropathy. In our study renal injury did not regress when plasma cholesterol levels were normalized. This low incidence of renal injury, without glomerulosclerosis, is probably in relationship with the not excessively high plasma cholesterol levels. Although the degree of renal injury seen in our study is modest, it indicated a potential relationship between lipids and a progressive renal disease.

Expression of β1- and β2-isoforms of the Na,K-ATPase during compensatory renal hypertrophy. *N. Eleno, A. Rodríguez-López, L.M. Díez-Panero, P. Martín-Vasallo, J.M. López-Novoa, Instituto Reina Sofía de Investigación Nefrológica; Departamento de Fisiología y Farmacología, Univ. Salamanca; Departamento de Bioquímica y Biología Molecular, Univ. La Laguna, Spain.* One of the main adaptative mechanisms following renal hypertrophy after a partial nephrectomy occurs with the sodium pump activity. However, at the moment it is unclear whether compensatory hypertrophy is associated to an increase in the number of the sodium pumps. There are few data about the evolution of α-subunit, but nothing has been found about the possible modification in the expression of β-subunit isoforms (β1 and β2). Therefore, we studied the differential expression of both β isoforms at the mRNA and protein levels in the renal cortex of the hypertrophied remnant kidney after unilateral nephrectomy. Under ether anesthesia, the left renal pedicle was ligated in male Wistar rats (253 ± 6.9 g) and the kidney excised through a lateral incision. All determinations were performed in the right kidney 1, 2, 3, 6, 10 and 13 days after left nephrectomy. Proteins and mRNAs were detected by Western and Northern blots, respectively, using well characterized polyclonal antibodies and cDNAs. Na,K-ATPase activity was determined as ATP hydrolysis in microsomes of renal cortex. The β subunit is a highly glycosylated peptide; to confirm the specificity of the bands in immunoblots, some protein samples were digested. The bands corresponding to the fully glycosylated peptides (molecular wt ~50) dissapeared after digestion revealing instead the core peptides (molecular wt ~35) and

partially deglycosylated isoforms. Right kidney hypertrophy after left nephrectomy was confirmed by comparing the total protein content and the following relationships: weight of the right kidney/weight of the animal, weight of the right kidney/weight of the left kidney. The specific enzymatic activity of the sodium pump increased on the third day in the cortex of the kidney undergoing hypertrophy. Immunoblots showed the expression of the $\beta 1$ glycopeptide in control kidneys until the 13th day. The relative density of the bands (the same amount of protein was charged in each lane) decreased the 1st, 2nd and 3rd days and recovered control values from the 6th day after uninephrectomy. The $\beta 2$ glycopeptide was only specifically detected the 3rd, 6th and 10th days after left nephrectomy. The signal for $\beta 1$ and $\beta 2$ mRNAs in the remnant kidney was maximal the 3rd and 6th days after contralateral nephrectomy. Therefore, the $\beta 1$ isoform was constitutively expressed in the kidney whereas the $\beta 2$ isoform was only expressed in the kidney undergoing compensatory hypertrophy.

Linkage analysis using α_{2A}-adrenergic receptor gene polymorphisms in families with essential hypertension. *J. Calls, S. Lario, A. Cases, M. Bono, J. Oriola, A. Torras, F. Rivera, A. Darnell, Nephrology Service and Hormonology Laboratory, Hospital Clínic i Provincial, Barcelona, Spain.* An increased platelet α_{2A}-adrenergic receptor (α_{2A}-AR) density has been described in nearly half of patients with essential hypertension (EH). Furthermore, an increased density of these receptors has been reported in normotensive children from hypertensive parents, suggesting that α_{2A}-AR may play a role in the genetic predisposition to hypertension. Our aim was to investigate the possible relationship between the increased α_{2A}-AR density and the haplotypes determined by the α_{2A}-AR gene polymorphisms in families with a positive history of hypertension. Six families with a positive history of EH were included, and they included at least two relatives with hypertension. α_{2A}-AR density and affinity were measured in intact platelets by radiolingand binding assay, using [^{3}H]-methylyohimbine as a ligand. The linkage analysis was performed with the three polymorphisms described for the α_{2A}-AR gene. Bsu36I and DraI polymorphisms were determined by Southern blot analysis following hibridization with a [^{32}P]-labeled ADRA2R probe. The third polymorphism was detected by PCR amplification and digestion with HhaI restriction enzyme. Twenty-two hypertensive and 9 normotensive subjects were included; 19 out of 22 hypertensive patients (86%) showed an increased α_{2A}-AR density [296 ± 14.5 binding sites per platelet (bsp)] compared to normotensives (162 ± 10.5 bsp, $P < 0.01$). The haplotypes for the α_{2A}-AR gene were informative in 4 out of 6 families, but no haplotype was associated to EH or the increased α_{2A}-AR density. Our results suggest that the genetic factor involved in the development of EH is not located in the α_{2A}-AR gene area. However, we cannot exclude the α_{2A}-AR gene as a candidate for EH, because of the low number of families analyzed.

Unsuspected renal artery stenosis in 418 patients with peripheral vascular disease. *R. Marín, C. Díaz-Corte, J. Cosío, J.E. Rodríguez, A. Valle, A. Barreiro, M. Sánchez, C. Glez-Portal, F. Fdez-Vega and J. Alvarez-Grande, Nephrology, Radiology and Vascular Surgery Services, Hospital Central de Asturias, Hospital Covadonga, Oviedo, Spain.* The aim of the study was to evaluate the prevalence of renal artery stenosis (RAS) in patients with peripheral atherosclerotic arterial disease and the clinical implications of this association. Between November 1993 and April 1995 we prospectively studied the prevalence of RAS in 418 consecutive patients undergoing angiography for peripheral vascular disease. We obtained information about the demographic data, the prevalence of cardiovascular risk factors, the serum creatinine level, the severity of vascular disease on the basis of angiographic findings (I to III categories) and the existence of another cardiovascular pathology. For statistical analysis patients were divided in two groups according to the presence or absence of RAS and the patients without RAS were the control group. RAS was detected in 114 patients (27%); in 24 patients it was bilateral and in 84 (74%) unilateral. The patients with RAS were older (72 ± 10 vs. 65 ± 12 years, $P < 0.001$), they had a higher prevalence of hypertension [59% vs. 36%, odds ratio (OR) 2.5, 95% confidence interval (CI) 1.6 to 3.9, $P < 0.001$], greater severity of arterial lesions in category III (66% vs. 38%, OR 3.1, CI 2.01 to 4, $P < 0.001$) and a higher serum creatinine level (1.44 ± 0.5 vs. 1.21 ± 0.3 mg/dl, $P < 0.001$). No differences were found in the prevalence of hyperlipidemia, diabetes or smoking. Patients with RAS had a greater prevalence of myocardial ischemia (26% vs. 13%, OR 2.4, CI 1.4 to 4.1, $P < 0.01$) and left ventricle hypertrophy (25% vs. 13%, OR 2.1, CI 1.2 to 3.6, $P < 0.05$). Using stepwise logistic regression analysis, the risk factors for RAS were the age, the presence of hypertension, the severity of peripheral vascular disease and the existence of ischemic heart disease. Hypertensive patients treated with angiotensin-converting enzyme (ACE) inhibitors had a higher serum creatinine level than hypertensive patients in therapy with others antihypertensive agents: 1.96 ± 0.8 vs. 1.54 ± 0.6, $P < 0.05$. Only when the stenosis was greater than 75% was hypertension and a higher serum creatinine level more prevalent. We conclude that there is an important prevalence of unknown RAS in patients with peripheral vascular disease. There is a direct relationship between the presence of RAS and the age, hypertension, severity of peripheral vascular disease and ischemic heart disease in these patients. Hypertensive patients with peripheral vascular disease who are treated with ACE-inhibitors had a higher serum creatinine level than hypertensive patients in therapy with others antihypertensive agents. The arteriography, as part of the routine evaluation for patients with atherosclerotic arterial disease, needs to include the study of renal arteries.

Is there a J-shaped curve of renal morbidity in treated elderly hypertensives? *P. Aranda, R. Marín, L.M. Ruilope, P. Aljama, M. Luque, on behalf of the Spanish Group. SEN and SEH, Madrid, Spain.* We investigated elderly patients who were diagnosed with mild to severe essential hypertension (EEH), independently of the type of antihypertensives used, and determined the effects of different degrees of blood pressure control on their renal function. In a cross sectional, observational, and national study on 2406 (62.8% females) treated EEH, men age 71.8 ± 7 years old, we evaluated the effects of different degrees of BP control on the lipid profile and renal function, measured by lipoprotein profile and serum creatinine levels, and the endogenous creatinine clearance using the Crockoft & Gault formula. After establishing the diagnosis of essential hypertension, we measured BP (mean of 2 readings), H.R. and BMI, as well as determined the levels of glucose in a fasting state, creatinine, t-cholesterol, triglycerides and lipoproteins. The mean time since the diagnosis of having EH was 88.6 ± 77 months. The mean values of BP in the treated hypertensives was 151.3 ± 12/87.4 ± 7 mm Hg, the mean BMI was 27.9 ± 4, mean serum Cr was 1.04 ± 0.31 mgdl and mean Cr clearance was 68.9 ± 20 ml/min. Antihypertensives used (%) included: ACEI, 47.4; CCB, 32.1; diuretics, 35.1; beta blockers, 6.1; and others, 9.44%. For the evaluation, the sample was divided according to the following BP levels: ≥ or <160/95 mm Hg and <135/85 mm Hg.

BP *mm Hg*	*N*	DBP *mm Hg*	SBP
<135/85	191	76.5 ± 6	129.9 ± 6
P		a	a
<160/95	1573	84.5 ± 8	151.2 ± 15
P		a	a
160/95	642	101.3 ± 6	175.9 ± 14

BP *mm Hg*	Creatinine *mg/dl*		C_{Cr} *<80 ml/min*
		>1.3	
<135/85	1.05 ± 0.23	19.4	79
P	c	c	c
<160/95	1.02 ± 0.32	14.4	73.3
P	c	a	NS
160/95	1.06 ± 0.28	20.07	70.4

BP *mm Hg*	LDL-cholesterol >165	Triglycerides >200
<135/85	34.1	13.9
P	c	NS
<160/95	45	11.8
P	a	a
160/95	54.5	17

(*)p < 0.001; (**)p < 0.01; (***)p < 0.05

We conclude that, independently of the antihypertensives used, the uncontrolled hypertensives (BP ≥ 160/95) as well as the elderly patients with a BP < 135/85 mm Hg had a worse renal function. Although it is necessary to perform longitudinal studies to corroborate these results, excessive BP control might contribute to a more rapid decline of renal function in treated elderly hypertensive patients.

Spiral computer tomography angiography (CTA): Utility for the diagnosis of renal artery stenosis. *C. García Ruiz, T. Sempere, A. Martinez, A. Ramos, J. Palao, C. Peralta, J.A. Oliver, Departments of Nephrology and Radiology, Universitary Hospital Joan XXIII, University of Tarragona, Spain.* Recently, the utility of spiral CTA has been demonstrated a new, minimally invasive technique with a sensitivity of 98% and specificity of 94% for the diagnosis of renal artery stenosis (RAS). To evaluate the accuracy of CTA in the diagnosis of RAS-induced hypertension, we studied 56 patients with suspected renal RAS, median age 56.1 years (19–78). Twenty-three of them had renal failure with a median serum creatinine of 229 μmol/liter (134–450). All of the patients had a spiral CTA done with a continuously rotating X-ray tube of 7–10 cm, slice thickness 2.7 mm, and a reconstruction interval of 1.4 mm. Contrast medium 2 cc/kg wt was injected intravenously with a flow rate of 4 cc/seg. Image analysis included not only a visualization of the axial images in a cine-mode, but also using interactive multiplanar reformatting, maximum intensity projections and three-dimensional reconstructions. The grading of stenosis was defined as: Grade 0, no stenosis; Grade I, stenosis <50%, Grade II, stenosis between 50–75%; Grade III, stenosis between 75–99%; Grade IV, occlusion. CTA was performed in 56 patients, 130 renal arteries were evaluated, 73% of them were normal, and stenoses of grade I to IV were detected in 27% of the renal arteries, 60% stenoses were grade I, 20% stenoses grade II, 14.2% grade III and 5.7% stenoses grade IV. In 19 patients with pathologic CTA arteriography was performed that showed the same stenoses grade in 16 and an overestimate in three. CTA was complicated by an allergic contrast reactions in one patient. We suggest that spiral CT angiography is a safe and minimally invasive method for the diagnosis of renal artery stenosis, and using this technique could lead to significant reductions in the number of diagnostic angiographies.

Prevalence and characteristics of diabetic nephropathy in diabetes mellitus secondary to alcoholic pancreatitis. *C. Morillas, A. Hernández, M.J. Morillas, J.L. Górriz, L.M. Pallardó, C. Catalán, D. Lorente, Departments of Endocrinology and Nephrology, Hospital Dr. Peset, Valencia, Spain.* The incidence of diabetic nephropathy (DN) in diabetes mellitus (DM) secondary to alcoholic pancreatitis remains controversial. A low prevalence has been reported in most of the studies, which could be due to a short follow-up of the patients, and the fact that most of the studies did not include microalbuminuria as marker for nephropathy. The aim of our study was to determine the prevalence and characteristics of DN in a group of pancreoprivic patients. We studied 40 patients (39 males and 1 female) with DM secondary to alcoholic chronic pancreatitis, diagnosed on the basis of clinical, morphological and functional criteria. Their mean age was 53 ± 8 years, mean alcohol consumption was 95 ± 62 g alcohol/day, and mean diabetes duration was 5.5 ± 3.6 years. HbAlc was 8.01 ± 2.29%. Microalbuminuria was determined by nephelometry, taking the average of three determinations after excluding urinary tract infection, hypertension and exercise before micturition. Values greater than 30 mg/24 hours were considered pathologic. Microalbuminuria was 260 ± 337 mg/24 hr, and >30 mg/24 hr in 21 patients (52.5%). Eight of them (20%) had established nephropathy (albuminuria >300 mg/24 hr) without renal insufficiency, and 13 patients (32.5%) showed albuminuria between 30 and 300 mg/24 hr. We conclude that the presence of diabetic nephropathy secondary to alcoholic pancreatitis is similar to that reported in primary diabetes mellitus, and it was related to diabetes duration. Chronic renal insufficiency is exceptional in DM secondary to alcoholic pancreatitis, probably due to its late onset and the short follow-up in this group low survival rate patients.

Thiazides plus enalapril can be safely used in hypertensive diabetics with nephropathy. *A.M. Castelao, M.T. González, Nephrology Department, H. Principes de España, CSU Bellvitge, University of Barcelona, Spain.* For years thiazides were not considered as a first-line choice of treatment for hypertension in diabetics, due to the possible deleterious effect on metabolic control (hyperglycemia, hyperuricemia, hypercholesterolemia). We investigated the long-term effect of treatment with enalapril, initially 20 mg/day, plus thiazide, 12.5 mg/day initial dose, in 24 patients with diabetic nephropathy (DN). Eleven were male and 13 female, mean age 57 ± 75 years, 5 with type I diabetes and 19 with type II diabetes. Blood pressure and biochemical parameters after 6 and 12 months of treatment were as follows:

	Before T.	6 months	12 months	*P*
Sysolic blood pressure	175 ± 25	156 ± 24	154 ± 23	0.001
Dyastolic BP *mm Hg*	89 ± 13	82 ± 10	78 ± 14	0.002
Urea *mmol/liter*	12.1 ± 4	12.6 ± 5	15 ± 8	0.009
Creatinine *μmol/liter*	175 ± 88	192 ± 98	208 ± 109	0.03
GFR *ml/min*	52.3 ± 24	44.8 ± 25	44 ± 26	0.002
Proteinuria *g/day*	3.07 ± 3.7	3.27 ± 4.4	2.18 ± 2.8	0.07
Glucose *mmol/liter*	10 ± 5.8	9.1 ± 4	9.3 ± 3.8	ns
A1c Hb %	7.6 ± 1.8	8 ± 1.4	7.8 ± 1.5	ns
Insulin dose *units/day*	22 ± 19	24 ± 19	25 ± 17	ns
Na *mmol/liter*	142 ± 3.9	140 ± 3	142 ± 3.9	ns
K *mmol/liter*	4.9 ± 0.5	4.8 ± 0.5	5 ± 0.7	ns
Uric acid *mmol/liter*	400 ± 98	420 ± 122	396 ± 94	ns
Total cholesterol *mmol/liter*	6.34 ± 1.1	6.06 ± 0.8	5.88 ± 1.2	0.06
Tryglicerides *mmol/liter*	2.4 ± 2.2	2.8 ± 2	2.3 ± 1.4	ns
HDL-chol. *mmol/liter*	1.01 ± 0.2	1.29 ± 0.4	1.09 ± 0.4	ns
LDL chol. *mmol/liter*	4.23 ± 0.68	3.65 ± 0.6	3.61 ± 0.8	ns
Hemoglobin *g%*	12.6 ± 0.2	11.9 ± 3	12 ± 2	ns
Fibrinogen *mg/liter*	6.12 ± 1.8	6.04 ± 1.3	5.65 ± 1.6	0.02
Enalapril dose *mg/day*	20 ± 8	24 ± 9	26 ± 7	ns
Thiazide dose *mg/day*	12.5 ± 6.2	14.8 ± 6.2	14.8 ± 6.2	ns

In spite of the increase in plasma urea and plasma creatinine and the decline of GFR, plasma potassium was maintained within normal range. All the patients but one showed good tolerance to the treatment. We stopped enalapril plus tyazide only in one patient, because of a skin rash after 3 months of therapy. In conclusion, thiazides in association with enalapril are well tolerated in DN patients without adding deletereous effects in the metabolic control of these patients.

Inhibition by enalaprilat of the hydrogen peroxide production by murine mesangial cells exposed to high glucose concentrations. *L.M. Ruiz-Muñoz, R. Muñiz, A. Solís, M.L. Muñiz, M.P. Martínez, I. Lampreabe, Department of Nephrology, Cruces Hospital; and Basque Country University, School of Medicine and Dentistry, Lejona, Vizcaya, Spain.* Angiotensin-converting enzyme (ACE) inhibitors are drugs with a well-known renal protective effect that is not fully related with its hypotensive action. The effect of enalaprilat on hydrogen peroxide (H_2O_2) production by cultured murine mesangial cells exposed to 5.5 (basal condition), 30 and 50 mM glucose concentrations was examined over 8 hours. The H_2O_2 was evaluated by microfluorimetry quantifying, in arbitrary units, the intracellular dichlorofluorescein (DCFH) oxidation to the highly fluorescent compound 2′,7′-dichlorofluorescein (DCF) from the non-fluorescent probe dichlorofluorescein-diacetate (DCFH-DA), incubated with mesangial cells (20 mM) for 20 minutes and washed before the addition of study conditions. Experiments were repeated three times in quadruplicate wells. H_2O_2 production by mesangial cells exposed to 50 mM glucose was significantly increased after one hour ($P < 0.05$) compared to cells exposed to 5.5 and 30 mM glucose. This observation was not reproduced with 50 mM mannitol. The addition of 100 ng/ml enalaprilat to cells with 50 mM glucose significantly inhibited H_2O_2 production over the 8 hours of the assay ($P < 0.01$). This response was similar to that obtained with 100 ng/ml catalase. Increasing enalaprilat concentrations (10, 50 and 100 ng/ml) also significantly decreased the constitutive H_2O_2 production with 5.5 mM glucose from the first hour ($P < 0.05$), the effect being more intense with 50 and 100 ng/ml at the 8th hour ($P < 0.01$). We conclude that the protective effect of enalaprilat may be related to an antioxidant action.

Analysis of percutaneous renal biopsy on allograft and native kidneys: Risks and benefits. *F.J. Gainza, J.I. Minguela, M.P. Martinez, M.L. Muñiz, L.M. Ruiz, I. Lopez-Vidaur, R. Muñiz, I. Lampreabe, Nephrology and Radiology Departments, Hospital de Cruces, Barakaldo, Bizkaia, Basque Country, Spain.* We conducted a prospective case-control study of the

complication rate following percutaneous renal biopsy (RB), which was ultrasound guided. We evaluated 225 consecutive biopsy procedures [122 on transplant kidneys (TK) and 103 on native kidneys (NK)]. Complications were evaluated by clinical, laboratory and ultrasonography studies using color-coded Doppler US as previously reported. Hospitalization time due to complications was recorded and economical considerations performed. The results were evaluated in a retrospective analysis by retrieving data from clinical records. The causes leading to RB in native kidney patients were: acute renal failure in 6 cases, rapidly progressive renal failure in 26, chronic renal failure in 12, nephrotic proteinuria in 53, and asymptomatic urinary abnormalities in 6. In transplanted patients the causes were: declining in renal function in 98 patients (47 from grafting to the first 3 months) and proteinuria in 24. In the paraffin sample there was (mean ± SD) 8.8 ± 0.5 glomeruli. Histological findings: (1) led to a new treatment in 24% of the cases, (2) confirmed one previously started treatment in 9%, and (3) changed the therapy regimen in another 9%. Taking NK and TK in comparison, renal biopsy provided therapeutic value in 47 and 38%, merely prognostic value in 45 and 57%, and was useless in 8 and 5%, respectively (χ^2; $P = 0.028$). Microscopic hematuria was the most frequent complication (22.6% of procedures). Regarding severe complications, bleeding (7.5%) and arteriovenous fistula (11.7%) were more frequent in allograft than in native kidneys ($P = 0.019$). There were neither nephrectomies nor deaths due to the RB. Twelve out of 84 patients (14%) admitted to perform RB remained hospitalized for a period of 5.6 ± 1.7 days due to complications. Percutaneous renal biopsy remains a useful procedure in at least 9 out of 10 patients, providing prognostic and/or therapeutic advantages. Severe complications occurred in less than 20% of procedures and they were more frequent in transplant patients.

Renal involvement in antiphospholipid syndrome without systemic lupus erythematosus. *A.E. Sirvent, R. Enríquez, C. González, J.B. Cabezuelo, A. Antolin, A. Teruel, A. Reyes, Nephrology and Pathology Sections, Hospital General de Elche, Spain.* There are scarce reports about nephropathy in antiphospholipid syndrome (AS) without underlying systemic lupus erythematosus (SLE). We describe the renal manifestations and the follow up of five patients with AS who were studied from 1991 to 1995 because of renal failure and/or high blood pressure. As was diagnosed according to Harris' criteria. No patient fullfilled ARA criteria for SLE. Lupus anticoagulant (LA) and anticardiolipin antibodies (aCL) were searched in the presence of prolonged aPTT, thrombocytopenia, thrombosis, livedo reticularis or hemolytic uremic syndrome (HUS). LA was determined by the Exner method or by a modified activated partial thromboplastin time; aCL were measured by ELISA. The age range of the patients, two women and three men, was 27 to 40 years. The span of the follow-up was between seven months and five years. Both LA and aCL were positive in three patients, only aCL in one and LA in another. The main extrarenal findings were: thrombocytopenia in five cases, thrombotic events (lower limb phlebitis, cerebral infarction, and celiac axis thrombosis) in three, and livedo reticularis in two. All the five patients had renal failure that followed an insidious course (serum creatinine stable around 1.5 mg/dl) in three cases. Two patients developed acute renal failure within HUS; one of these presented oliguria requiring hemodialysis, although afterwards her renal function improved (C_{Cr} 30–40 ml/min), the other one with malignant hypertension needed hemodialysis from the beginning. Arterial hypertension of different severity, from mild to malignant, was a general feature. Non-nephrotic proteinuria was present in four patients, the urinary sediment revealed no abnormalities in four cases and microscopic hematuria in the other. Renal angiography, made in four patients, disclosed no significant changes. Kidney biopsy, performed in four cases, showed a non-inflammatory microangiopathy, with variable severity and chronicity; immunoglobulins and complement deposits were not seen by immunofluorescence study. All the patients were treated with antiplatelet agents, one received warfarin, plasma exchanges were used in the two HUS and steroids were initially given to two. We conclude the following. (1.) The renal failure in AS revealed, generally, a non-inflammatory microvascular nephropathy. (2.) LA and aCL need to be determined in HUS. (3.) Arterial hypertension, even with normal renal arteries, is a frequent feature of AS and may be malignant. (4.) The therapy of AS nephropathy consists of oral anticoagulants and antiplatelets agents; the best treatment is not established, and it might be individualized according to the extrarenal events and the way and severity of its presentation.

Anti-neutrophilic citoplasmic autoantibody-associated Glomerulonephritis. Clinical course and disease activity follow-up. *M.T. Hernandez, J.R. Gomez-Martino, I. Castellano, A. Covarsi, R. Novillo, N. Marigliano, O. Sanchez, Hospital San Pedro de Alcantara, Caceres, Spain.* We have reviewed the ANCA and associated glomerulonephritis seen in our unit between October 1990 and December 1995 (63 months). We performed a total of 160 renal biopsies, of which 23 (14%) were ANCA associated GN: 10 idiopatic extracapillary glomerulonephritis and 13 GN secondary to systemic vasculitis (2 Wegener's granulomatosis, 1 classic PAN, 10 microscopic PAN). All patients were treated with bolus of 6-metil prednisolone that was followed by prednisone and oral cyclophosphamide. Nine patients received additional treatment with plasmapheresis). Three patients didn't receive treatment, two for death before starting the regimen and one because he presented with severe damage of chronicity in the renal biopsy. ANCA was reasured by RIA being 19 p-ANCA and 4 c-ANCA. The follow-up was 14.8 months (20 days to 63 months). Of the 23 patients, 5 recovered "ad integrum" the renal function, 3 live with a mild chronic renal failure (Crp < 2 mg/dl), one other patient had a moderate chronic renal failure (Crp 2–4 mg/dl), 6 progressed to ESRD severe enough to start renal replacement therapy, and 8 died by their illness or complications. The necrosis of the tuft, crescents in an upper 50%, and the existence of diffuse alveolar hemorrhage were signs of bad outcome. Differences between the patients treated with plasmapheresis or without it were nonexistant. The follow-up of ANCA was made in 19 patients; 17 of them (89%) were negative 3–54 months after the beginning of treatment. We observed a rise in the ANCA titers, without evidence of clinical activity in 3 patients. In conclusion, (1.) The percentage of ANCA-associated glomerulonephritis in our unit in the studied time was 14%. The most frequent association was with p-ANCA (82%) and the bigest incidence of presentation was during March–April. (2.) The parameters that established a bad outcome has been glomerular necrosis, crescents in a percentage more than 50% and the existence or not of alveolar hemorrhage. (3.) The global patient survival rate at the end of the 63 months was 65%. We didn't find differences between patients with illnes autolimited to kidney or those with systemic vasculitis. (4.) There weren't differences between renal survival and patient survival when they received treatment with plasmapheresis or not.

Chronic nephrotoxicity caused by cyclosporine A. Role of endothelin in the induction of interstitial fibrosis. *C. Ramírez, A. Olmo, M. Andujar, F. O'Valle, F. Revelles, M.J. García-Chicano, D. Aguilar, M. Aguilar, R.G. Del Moral, Department of Pathology, University Hospital, Granada, Spain.* Chronic nephrotoxicity (CNT) caused by cyclosporine A (CsA) is characterized by progressive renal insufficiency accompanied by interstitial fibrosis and tubular atrophy. Although increased endothelin (Et) is known to induce chronic ischemia, and may be important in the genesis of CNT, other mediators of fibrogenesis have been implicated, such as, TGF-β and angiotensin II. We studied the secretion of Et1 and Et3 in the renal parenchyma with immunohistochemical methods, and determined the expression of mRNA with Northern blotting, in an experimental model of CNT in Sprague-Dawley rats. We studied 20 animals divided into three groups: CsA-treated (25 mg/kg/day), Cremophor-treated, and saline solution-treated (control), for 2 months. Histological lesions were evaluated with conventional methods (vacuolization and tubular atrophy), and interstitial fibrosis was quantified with an automatic image analysis method (Fibrosis HR software, Master Diagnóstica, Spain). Et1 and Et3 were determined immunohistochemically with a specific polyclonal antibody (Peninsula Laboratories, USA). Treated animals showed significant increases in BUN and serum creatinine, and in characteristic tubulointerstitial lesions including a greater percentage of fibrosis, in comparison with control animals. There was a general increase in Et1 and Et3 in glomeruli and tubules, although immunostaining for Et3 [glomeruli, 4.7 ± 1.3 (range 3–9) vs. 4.1 ± 1.5, ANOVA $P < 0.01$; tubule, 2.7 ± 0.6 (range 1–4) vs. 2.2 ± 0.8, ANOVA $P < 0.05$] was greater than for Et1 [glomeruli, 4.9 ± 1.7 (range 3–9) vs. 5.4 ± 1.8; tubule, 2.8 ± 0.8 (range 1–4) vs. 2.5 ± 0.6]. The relation between increased Et3 deposits and histological lesions was highly significant (interstitial fibrosis 9.0 ± 1.7% with slight deposits, vs. 11.7 ± 0.8% with heavy deposits, ANOVA $P < 0.05$). This relationship was not found for Et1 deposits. The expression of mRNA for both Et1 (0.47 ± 0.19 vs. 0.33 ± 0.04) and Et3 (0.31 ± 0.18 vs. 0.23 ± 0.08) was increased in CsA-treated rats vs. controls; this difference was significant for Et1. In conclusion (1) in CNT caused by CsA, the intrarenal secretion of Et is increased; this effect is related with the severity of histological

lesions. (2) Increased Et3 (immunohistochemically determined) suggests that this substance plays an important role as a paracrine inducer of fibrosis in CsA-caused CNT. (3) The increase in mRNA for Et1, which was not accompanied by a notable increase in immunohistochemical findings, suggests that this mediator is released actively and rapidly into the vascular spaces of the kidney, and that it may play an important role in the ischemia that accompanies CsA-caused CNT.

Current use of renal biopsy in acute renal failure (ARF). Data from a multicenter survey. *J. Pascual and F. Liaño for the Madrid ARF Study Group, Department of Nephrology, Hospital Ramón y Cajal, Madrid, Spain.* Renal biopsy has had fluctuating roles in the diagnostic work-up of ARF. After non-renal causes of ARF are excluded, the most common etiologic factor of ARF is acute tubular necrosis (ATN). Patients with well-established clinical and laboratory features of ATN receive no benefits from a renal biopsy. Current performance of renal biopsy in community-based studies including wide populations with ARF is not known. The 13 tertiary-care hospitals in Madrid (covered population 4.2 million people over 14 years of age) underwent a prospective study of all ARF cases, including a number of clinical and laboratory variables. ARF was diagnosed when a sudden rise in serum creatinine to more than 177 μmol/liter was found in patients with normal renal function or when the sudden rise was observed in patients with previous mild-to-moderate chronic renal failure (CRF). Absolute freedom for diagnostic work-up and treatment of ARF was instituted by the study group. During 9 months 748 cases of ARF were attended, an incidence of 209 cases p.m.p. Etiologies were ATN (45%), prerenal (21%), acute onset of CRF (13%), obstructive (10%), other (11%). Renal biopsy was performed in 46 patients (1 each 16 cases). In 4 cases the patient had acute onset of CRF. Histologic diagnoses were primary glomerulonephritis (GN) ($N = 12.26\%$), vasculitis ($N = 10.22\%$), secondary GN ($N = 6$, 13%), ATN ($N = 4.9\%$), acute tubulointerstitial nephritis (ATIN) ($N = 4.9\%$), atheroembolic disease ($N = 2.4\%$), myeloma ($N = 2.4\%$), other ($N = 6.13\%$). Comparing with overall etiologies and incidences, all primary GN, 90% of vasculitis and 50% of secondary GN cases were diagnosed by biopsy at the time of ARF. Up to 15 patients were diagnosed as having ATIN, but only 4 (27%) were biopsied. Only 4 of 337 patients with ATN (1.2%) underwent biopsy. Renal biopsy has very limited indications in ARF. Only 6% of ARF patients evaluated in 13 tertiary-care hospitals required it for accurate assessment. A renal biopsy may be performed only to establish a specific diagnosis such as acute or rapidly progressive GN, vasculitis or ATIN, for cases in which an accurate diagnosis cannot be made clinically.

Increased glomerular nitric oxide synthesis in ischemic acute renal failure. A role for uremia. *J.M. Valdivielso, L. Rivas-Cabañero, M. Arévalo, C. Crespo, J.R. Alonso, J.M. López-Novoa, Instituto Reina Sofía de Investigación Nefrológica, Departamento de Fisiología y Farmacología, Departamento de Anatomía Humana e Histología, Departamento de Biología Celular y Patología, Universidad de Salamanca, Salamanca, Spain.* Previous works from our laboratory showed an increase in glomerular nitric oxide synthesis in a model of 1 hour of ischemia and 24 hours of reperfusion, but not in another group of rats which had the same time of ischemia and 2 hours of reperfusion. The aim of this study was to determine if it is the ischemia or the uremia the responsible for this increased nitric oxide synthesis. Ischemia was induced by clamping one or both renal arteries. Also, nitric oxide synthesis was inhibited by adding L-NAME (4 mg/k/day) in the drinking water. Groups resulted as follows: S Group, sham operated rats; SN group, sham operated rats with L-NAME in the drinking water; BI group, rats with bilateral ischemia; BIN group, rats with bilateral ischemia and L-NAME in the drinking water; UI group, rats with unilateral ischemia; UIN group, rats with unilateral ischemia and L-NAME in the drinking water. Renal function was measured in all the groups 24 hours before and after inducing the ischemia. Glomeruli from rats which did not drink L-NAME were isolated at the end of the treatment and glomerular nitrite production was determined (in the UI group glomeruli were isolated separately from ischemic and nonischemic kidney). Also, a hystochemistry for NADPH diaphorase activity and an immunohystochemistry for inducible nitric oxide synthase (iNOS) were made in slices of kidneys from rats which did not drink L-NAME; a Western blot analysis for the same protein was also made in glomeruli from these groups. A histologic study was also made in all the groups, staining the slices with the PAS technique. Only glomeruli from rats of the IB group showed an increase in nitrite production and NADPH diaphorase activity. iNOS was neither detected with Western blot nor by immunohystochemistry. After L-NAME treatment, morphological and functional damage was more severely aggravated in the BI group than in all the others. All these results suggest that the increased nitric oxide synthesis observed in ischemic acute renal failure is due to both ischemia and the developing uremia, and that this increase is not due to the iNOS activity. The increased nitric oxide synthesis plays a protective role in ischemia-induced renal damage.

Involvement of phospholipase A_2 in gentamicin-induced rat mesangial cell activation. *C. Martínez-Salgado, A. Rodríguez-Barbero, D. Rodríguez-Puyol, M. Rodríguez-Puyol, J.M. López-Novoa, Instituto Reina Sofía de Investigación Nefrológica, Departamento de Fisiología y Farmacología, Universidad de Salamanca, Salamanca, and Departamento de Fisiología, Universidad de Alcalá de Henares, Madrid, Spain.* Gentamicin induces mesangial cell contraction and proliferation; both effects seem to be mediated, at least in part, by platelet activating factor (PAF). Phospholipase A_2 (PLA_2) is a membrane-associated enzyme involved in prostaglandins and PAF synthesis. We have studied the role of PLA_2 in the gentamicin-induced mesangial cell activation. The decrease in planar cell surface area induced by gentamicin (10^{-5} M), after 60 minutes of incubation, was partially blocked by a PLA_2 inhibitor, aristolochic acid (AA) (1.5×10^{-4} M), by a PAF blocker, BN-52021 (BN) (5×10^{-5} M) and by a calcium channels antagonist, verapamil (V) (10^{-5} M). These substances also inhibited the effect of gentamicin on ^{3}H-thymidine incorporation into DNA, and on cell proliferation. The two-fold increase on ^{3}H-acetate incorporation into PAF induced by gentamicin was completely blocked by AA, BN and V. When PAF was added in addition with gentamicin, there was a threefold increase on ^{3}H-acetate incorporation into PAF. Gentamicin increased the TXB_2 and PGE_2 production by mesangial cells; these increases dissappeared in the presence of either AA or V. BN diminishes the PGE_2 production induced by gentamicin, but there was no effect on TXB_2 production. When PAF was added in addition with gentamicin, the TXB_2 and PGE_2 production were increased eight- and fourfold, respectively. The present study demonstrates that gentamicin-induced rat mesangial cell activation is mediated, at least in part, by the activation of PLA_2.

Decreased acute renal failure (ARF) following allogenic bone marrow transplantation (TMO) with use of imipenem-cilastatin. *E. Gruss, C. Bernis, J.F. Tomás, F. Salvanés, J.L. Motellón, A. Figuera, E. Muñoz, G. Barril, J.A. Sánchez-Tomero, V. Alvarez, J.M. Fernández-Rañada, J.A. Traver, Departments of Nephrology, Hematology and Investigation Unit, Hospital de la Princesa, Madrid, Spain.* ARF is a common complication following allogenic BMT. The veno-occlusive disease (VOD) and cyclosporine (CsA) use are correlated with this finding. Cilastatin an inhibitor of the tubular brush border enzyme dehydropeptidase is a added in a fixed combination to antibiotic imipenem. Cilastatin has been demonstrated in different animal models and in one clinical trial to reduce the nephrotoxicity associated with CsA by two mechanisms: preventing intracellular accumulation of CsA and/or stimulating hepatic metabolism. To evaluate a possible nephroprotective effect of cilastatin following allogenic BMT we conducted a retrospective analysis of 104 patients transplanted from January 1991 to January 1995. ARF was defined by two conditions: at least a doubling of baseline creatinine and by reaching levels higher than 2 mg/dl. Imipenem/cilastatin (I/C) was employed in 64 patients along that period. ARF was diagnosed in 32 patients (30%). ARF was not associated with sex distribution, sepsis, conditioning regime, underlying disease and age. Veno-occlusive disease was presented in 12/32 (37.5%) of patients with ARF, whereas it was presented in only 7/72 (9.7%) of patients without ARF ($P < 0.0007$). Neither ARF was correlated with aminoglycosides, vancomycin, ciprofloxacine, ceftazidime and amphotericin-B. However, 13 patients of 64 exposed to I/C (20.3%) developed ARF versus 19 of 40 (47.5%) who were not exposed to I/C ($P < 0.003$; OR 0.28). The mean cyclosporine levels in I/C group were significantly decreased (208.6 ± 64.9) versus non-I/C group (265 ± 118). We conclude that these results suggest I/C could counteract acute cyclosporine nephrotoxicity following BMT.

Is survival in acute renal failure patients requiring hemodialysis dependent on the type of membrane used? *F. Liaño and J. Pascual for the Madrid ARF Study Group, Department of Nephrology, Hospital Ramón y Cajal, Madrid, Spain.* Recent published data have pointed out significantly

higher survival with biocompatible membranes in conventional hemodialysis for acute renal failure (ARF). The hypothesis in these studies is that the use of synthetic, biocompatible membranes will reduce mortality. During a 9-month period, a collaborative prospective protocol was developed to assess all ARF episodes attended in the 13 tertiary-care hospitals in Madrid (covered population 4.2 million people over 14 years old). One of the objectives was to assess the influence of the type of membrane used in survival of ARF patients requiring acute hemodialysis. During the study period, ARF was diagnosed in 748 patients and 270 of them (36%) needed dialysis. Conventional hemodialysis was used in 162 and other techniques in the remainder. In 134 of the conventionally hemodialyzed patients the type of membrane was recorded and constitute the study group:

	Cellulosic ($N = 84$)	Synthetic ($N = 50$)
Survivors N %	34 (40.5)	17 (34)
Nonsurvivors N %	50 (59.5)	33 (66)
Severity index[a]	0.52 ± 0.24	0.47 ± 0.26
Number of procedures	6.5 ± 7.0 (1–34)	6.5 ± 7.4 (1–36)

[a] According to our equation (*Nephron* 63:21–31, 1993)
All comparisons between both groups were not significant.

Our multicenter ARF study did not confirm higher survival with biocompatible membranes in conventional hemodialysis for ARF. Mortality was similar with cellulosic and synthetic membranes, with comparable severity of ARF episodes in both groups. The effect of dialysis membrane on survival is open for further research.

Predictive value of APACHE II score in acute renal failure (ARF) in the intensive care unit (ICU). *E. Verde, F. Ruiz, M.C. Vozmediano, I. Lorenzo, R. Pérez, E. Junco, P. Rodríguez, L. Inchaustegui, J.E. Guerrero, F. Valderrábano, Department of Nephrology and Intensive Care, Hospital General "Gregorio Marañón," Madrid, Spain.* The APACHE II score is a prognostic index used in critically ill patients. However, the predictive value of APACHE II in ARF is still unclear. Fifty-five patients (40 M/15 F; mean age = 62 ± 13 years) with ARF admitted into medicosurgical ICUs of our Hospital were prospectively analyzed for 6 months. APACHE II scores were determined at the initial clinical evaluation for nephrologists. Twenty-two patients (40%) required dialytic treatment (Group A) and the remaining 33 (60%) did not need it (Group B). There were no differences in age, sex and etiology of ARF between groups. Acute tubular necrosis was the more frequent cause of ARF in the two groups (72% and 54%). Continuous renal replacement therapies were the most used in the treatment for critically ill patients (76%), followed by intermittent hemodialysis (20%). Mortality rate was higher in group A compared to group B (68% vs. 42%; $P < 0.05$), but no differences were found in APACHE II scores between groups (22 ± 6 vs. 22 ± 6). This score was useful to predict outcome in group B (survivors 19 ± 8 vs. non-survivors 26 ± 4; $P < 0.01$). However, no differences were found in group A (survivors 20 ± 5 vs. non-survivors 23 ± 7; NS). Prediction of mortality could be made in group A with a sensitivity and specificity of 60% and 57%, respectively, when selecting a cutpoint that maximized both. In contrast, sensitivity and specificity were 93% and 68%, respectively, in the other group. In conclusion, APACHE II score is a useful prognostic index in non-dialyzed patients with ARF; however, this score has a poor predictive value in dialyzed patients.

Register of 319 central venous catheters (CVC): Complications and their actuarial survival in an acute care unit of nephrology. *A. Solís, J.I. Minguela, F.J. Gainza, J.M. Urbizu, J.J. Amenabar, I. Lampreabe, Nephrology Department, Cruces Hospital, Baracaldo, Bizkaia, Basque Country, Spain.* The arteriovenous fistulae of Cimino-Brescia is established as the preferred blood access method for hemodialysis (HD). However, the required maturation or the difficulty of a surgically created vascular access being available makes the use of CVC necessary. In order to evaluate the complication rate and actuarial survival of catheters (Kaplan-Meier method) a register was established and 319 successive CVC who were placed or rechanged to the Seldinger technique were followed through in 171 patients from June 94 to March 96 (age range 16 to 85 years). The CVC was placed for chronic HD (41%), intermittent acute HD (18%), continuous HD (31%) or other uses (10%). The preferred localization was the right femoral vein (40.9%), followed by right subclavian (13.8%), right jugular (13.2%), left subclavian (8.8%), left jugular (5%) and femoral artery for HDCAV (0.6%). The temporal accesses were made of polyurethane, all of them except 4 were double lumen. Regarding the length, 238 were of 20 cm, 77 of 15 cm and 4 longer than 20 cm (subcutaneous soft silicon rubber catheters for long-term dialysis). The CVC actuarial survival at the end of 7 days was of 65%, 14 days 48%, 21 days 34%, and a month 21%; the right jugular route of access presented significantly the best results. The main cause of catheter removal was flow dysfunction (33%). The main complications were: 22 infection episodes, venous thrombosis due to CVC in 5 cases, hemorrhage or significant hematoma in 6 (2.1%), pneumo- or hemothorax in 3 (1%). Two deceases were directly attributed to the procedure of insertion (a jugular attempt with carotid tear and a femoral artery for HDCAV with peritoneal hemorrhage). We conclude that the preferred site for CVC is the femoral vein and the right side is preferred in all circumstances. The CVC actuarial survival at the end of a month is low, and the right jugular presented the best results. Severe complications appeared in more than 10% of the cases with fatal results in almost 1% of the procedures.

Effect of the treatment with verapamil, trandolapril and veratran on glomerulosclerosis development in rats with 5/6 nephrectomy. *O. Flores, S. Vidal, M. Arévalo, B. Gallego, F. Hidalgo, and J.M. López-Novoa, Instituto Reina Sofía de Investigación Nefrológica, Departamento de Fisiología y Farmacología, Departamento de Anatomía e Histología Humanas, Facultad de Medicina, Universidad de Salamanca, Salamanca, Spain.* The aim of this study has been to assess the effects of the addition of a calcium channel blocker, verapamil, at a nonhypotensive dose (20 mg/kg/day) to an ACE inhibitor, trandolapril, at a hypotensive dose (0.7 mg/kg/day) on glomerular and interstitial fibrosis in rats with 5/6th nephrectomy. Trandolapril markedly increased the survival ratio, which after six months reached 87%. No mortality was observed in rats treated with the combination of verapamil and trandolapril. Trandolapril treatment prevented the development of hypertension. The combination of verapamil with trandolapril did not induce a further reduction on systolic or diastolic blood pressure, as compared with trandolapril alone. Control untreated group showed an urinary protein excretion that was increasing with time, reaching values 320.2 ± 54.7 mg/day after six months of follow-up. The trandolapril group showed an important reduction in proteinuria and it was maintained in treatments of 70 mg/day. The verapamil + trandolapril group showed a proteinuria significantly smaller than that of all the other groups (25.9 ± 9.45 mg/day) at the end of the study. Morphological studies by light microscopic analysis showed that more than 70% of the glomeruli showed sclerotic lesions in the control group. Interstitial fibrosis was observed mainly located around the more severed damaged corpuscles and tubules. The trandolapril group had a marked reduction in glomerular and tubulointerstitial alterations, while the verapamil + trandolapril group had a preserved architecture and tubulointerstitial space alterations were markedly reduced in most glomeruli. Quantitative determinations of glomerular (GF) and interstitial fibrosis (IF) performed with the sofware Fibrosis. HR (Master Diagnóstica®) on Syrium red stained renal sections, demonstrated that intraglomerular (GF) and interstitial fibrosis (IF) were reduced when rats were treated with trandolapril (GF = 2631 ± 62 μm^2, IF = 68736 ± 214 μm^2) and especially with verapamil + trandolapril (GF = 2287 ± 47 μm^2; IF = 5665 ± 154 μm^2) when they were compared to untreated animals values (GF = 3063 ± 65 μm^2; IF = 9359 ± 331 μm^2). Verapamil treatment neither reduced glomerular fibrosis (GF = 3230 ± 65 μm^2) nor interstital fibrosis (IF = 12271 ± 492 μm^2). We conclude that verapamil given in addition to trandolapril produces additional protection against progressive renal injury associated to subtotal nephrectomy, a protection that cannot be explained by a further decrease in arterial pressure.

Oxidative stress in patients undergoing hemodialysis. *M.J. Barrero, M.C. Martín Mateo, E. del Canto, J. Bustamante, A. de Paula, Department de Bioquímica, Facultad de Ciencias, Universidad de Valladolid, Hospital Clínico Universitario de Valladolid, Spain.* We studied the possible oxidative stress suffered by patients with chronic renal failure undergoing peritoneal hemodialysis and dialysis, relating to three types of membrane in order to better understand their biocompatibilities. In this way, concentrations of malonildialdehyde in these patients red blood cells were

considered a highly significant index to show cellular membrane lipid perioxidation. Malonildialdehyde concentrationes in patients are then used first to analyze the three forms of glutation (total glutation, oxidase glutation and reduced glutation), and secondly, to analyze the biomolecules in charge of both maintaining cell permeability and preventing Fe^{++} from oxidizing into Fe^{+++} in the hemoglobin. Finally we investigated peroxidase glutation concentrations in red blood cells and in these patients' plasma. By comparing the values obtained from a control group of blood donors, we observed that glutation values are much lower, and that the molonildialdeyde values are much higher than those in the control group of blood donors. Accordingly, peroxidase glutation concentrations in plasma are smaller, especially in the CAPD, and most significantly of all, in the red blood cells. These results indicate that these patients suffer from an important oxidative stress.

Expression of activation antigens CD25 and HLA-DR in the TCR$\alpha\beta$+ and TCR$\gamma\delta$+ peripheral blood T-lymphocytes: Immunomodulatory effects of dialysis. *A. Gascón, A. Orfao, J. Lerma, J. Ciudad, A. López, E. Iglesias, J.M. Tabernero, S. of Nephrology and Cytometry, University Hospital, Salamanca, Spain.* Little is known about the uremia and dialysis immunomodulatory effects in the TCR/CD3 receptor complex, which represents a key molecule in the process of antigen recognition and T-cell activation. In addition, both a major defect in the accessory cell system and a state of uremic-induced T and NK-cell preactivation have recently been found in these individuals. The aim of the present study was to analyze the coexpression of the CD25 and HLADR activation-associated antigens in both the TCR$\alpha\beta$+/CD3+ and the TCR$\gamma\delta$+/CD3+ T-cells in both patients in ESRD and individuals undergoing dialysis (CAPD and HD). A total of 42 patients (9 in ESRD, 8 in CAPD, 25 in HD; 14 with cuprophan and 11 with biocompatible membranes) were studied. A group of 18 healthy voluntcers was analyzed as controls. PB samples were analyzed at flow cytometry using a panel of direct conjugated monoclonal antibodies with FITC, PE and Per-CP, against CD3, TCR$\alpha\beta$, TCR$\gamma\delta$, CD25 and HLA-DR antigens. Patients on ESRD and undergoing dialysis (CAPD and HD) showed a marked decrease ($P < 0.0001$) in the absolute number of PB lymphocytes with respect to the controls. The distribution of the T-cell subsets analyzed are shown in the following table (absolute numbers and percentage of total either the T$\alpha\beta$ or the T$\gamma\delta$ subpopulations in brackets):

	TCR$\alpha\beta$+	$\alpha\beta$CD25+	$\alpha\beta$DR+
CONT	1439	347 (24%)	153 (11%)
IRCT	1030	267 (26%)	192 (19%)
CAPD	954	349 (37%)	164 (17%)
HD	960	365 (38%)	138 (14%)
CUP	908	361 (40%)	137 (15%)
BIOC	1026	368 (36%)	139 (13%)
ANOVA-test		$P < 0.01$	$P < 0.01$

	TCR$\gamma\delta$+	$\gamma\delta$CD25+	$\gamma\delta$/DR+
CONT	78	18 (23%)	10 (13%)
IRCT	104	5 (5%)	25 (24%)
CAPD	43	4 (9%)	9 (21%)
HD	32	4 (13%)	5 (16%)
CUP	27	5 (19%)	4 (15%)
BIOC	39	3 (8%)	6 (15%)
ANOVA-test			$P < 0.01$

In summary, our results show that there is an increased percentage of T-cells that coexpress the CD25 and HLA-DR activation antigens in patients undergoing dialysis; this rise of CD25 and HLD-DR expression is greater with cuprophan membrane HD and CAPD, respectively. Interestingly, the expression of the HLA-DR antigen on both the $\gamma\delta$ and $\alpha\beta$ T-cell subsets, but not the CD25 antigen, is also increased in the ESRD group of patients. These results indicate that ESRD and dialysis induce an activation of both the $\alpha\beta$ and $\gamma\delta$ T-cells, although a different pattern of reactivity for the CD25 and HLA-DR antigens is detected, suggesting that different mechanisms may be involved on the activation of $\alpha\beta$ and $\gamma\delta$ T-cells in both pathologic conditions.

Differentiation by flow cytometry of peripheral blood cells with natural killer cell activity in uremic and dialysis patients. *A. Gascón, A. Orfao, J. Lerma, J. Ciudad, A. López, E. Iglesias, J.M. Tabernero, S. Nephrology and Cytometry, University Hospital, Salamanca, Spain.* The antigens used most extensively as NK-cell "markers" are CD56 and CD16. CD3 is not present on NK cells, which do not rearrange TCR genes nor express T cell receptor heterodimers. Most CD56+ peripheral blood (PB) NK-cells coexpress CD16, and the remaining cells mainly corresponding to the CD16− CD56+ phenotypes. Whether this NK-cell subset represents the precursors of the more numerous CD56+ CD16+ NK cells or are a discrete NK cell subpopulation with unique functional attributes is presently unclear. The aim of the present study was to analyze both the distribution of different NK-cell subsets (CD3−CD16+ CD56+,CD3−CD16+CD56−, CD3−CD16−CD56+) and their functional cytotoxic activity in the PB of patients with ESRD and patients on dialysis (CAPD and HD). A total of 42 patients (9 in ESRD, 8 in CAPD, 25 in HD; 14 with cuprophan and 11 with biocompatible membranes) were studied. A group of 18 healthy controls was also analyzed. PB NK-phenotypes were analyzed at flow cytometry, and NK-cell activity was evaluated by a conventional cytotoxicity assay. Both the ESRD patients and the individuals undergoing dialysis showed a marked lymphopenia ($P < 0.0001$) with respect to controls. Mean values expressed as absolute numbers and percentages of the total NK-cells were as follows:

	Total NK	CD16+CD56+	CD16+CD56−	CD16−CD56+
CONT	351	301 (87%)	30 (8%)	20 (5%)
IRCT	224	174 (77%)	21 (10%)	28 (13%)
CAPD	176	78 (44%)	26 (15%)	72 (41%)
HD	191	97 (49%)	39 (20%)	61 (31%)
CUPR	170	79 (44%)	42 (23%)	60 (33%)
BIOC	214	117 (54%)	36 (17%)	61 (29%)
ANOVA:	$P < 0.01$	$P < 0.001$	$P < 0.04$	$P < 0.003$

In addition, the NK activity was directly correlated with the CD3−CD16+CD56+ NK-cells ($P < 0.001$) in patients undergoing dialysis. In summary, our results show that dialysis as compared with ESRD elicits a greater redistribution of the PB NK-cell subsets, with a marked decrease of the mature CD3−CD16+CD56+ cells. A significant increase is seen in the inmature or precursor CD3−CD16−CD56+ NK compartment in patients on dialysis. There is no correlation between these cells and NK-cell activity in dialysis patients. These findings confirm the possible existence of a correlation between antigen phenotype and NK-cell activity.

Prevalence of hepatitis C virus in pre-dialysis patients in 25 Spanish hospitals. Spanish multicentric study. *G. Barril and J.A. Traver (Coordinators), Hospital de la Princesa, Madrid, Spain.* There is a high incidence of new HCV positive patients initiating renal replacement therapies (RRT) each year. Therefore, we decided to study the prevalence of HCV antibodies in predialysis patients to analyze the potential risk factors involved in its infection. We studied 709 patients with creatinine clearance less than 20 ml/min from 25 Spanish nephrology departments. In every patient, we have analyzed age, sex, cause of end-stage renal failure (ESRF), time to develop ESRF, HCV antibodies, screening and confirmation test, antecedents of hepatopathy, blood transfusions, surgery, catheterization and hepatic or renal biopsy. The prevalence of HCV antibodies in pre-dialysis patients was 7.9% compared to 1.2% in our healthy population.

	HCV Ab (+)	P	HCV Ab (−)
Mean age	54.4	NS	57.4
Sex: male %	78%	0.05	60%
female %	22%	<0.05	40%
Months to ESRF	93.5	NS	94.4

There is a statistically significant difference between both groups regarding antecedents of blood transfusions and the number of them. Antecedents of surgery appears in 70% of HCV (+) patients compared to 30% of VHC

(−). The percentage of HCV (+) patients with ESRF caused by glomerulonephritis is also higher ($P < 0.05$). A total of 77% of VHC (+) patients had no history of clinically evident acute hepatitis, and 78% of the ultrasound studies performed in 60 VHC (+) patients were considered normal. Hepatic biopsy revealed cirrhosis in 5 patients and chronic active hepatitis in 1. We conclude that a higher prevalence of VHC antibodies in pre-dialysis patients exists compared to healthy population. The number of blood transfusions received and the antecedent of surgery seem to be risk factors to HCV infection. There is not any difference between HCV (+) and HCV (−) patients regarding age, but it seems that HCV (+) antibodies are more frequent in male patients and those whose ESRF is secondary to glomerulonephritis.

Effect of antihypertensive treatment on progression of renal insufficiency in non-diabetics patients (Espiral Trial). *R. Marín, L.M. Ruilope, P. Aljama, P. Aranda, J. Díez, on behalf of the 26 participating centers, Sociedad Española de Nefrología, Sociedad Española de Hipertensión.* A three-year long-term randomized, multicenter and prospectively opened trial is being developed with the aim of studying the influence of antihypertensive therapy on chronic renal failure progression in non-diabetic patients. The study will compare the effects of an angiotensin converting enzyme inhibitor, fosinopril, with a slow release calcium antagonist, nifedipine GITS. Two hundred and fifty patients, with progression of renal function decline, evidenced by an increase of serum creatinine (S_{Cr}) of at least 25% in a period of 2 years preceding study entry, and S_{Cr} levels between 1.5 and 5.0 mg/dl, will be included. The primary end point of the trial will be to compare the evolution of S_{Cr} (mg/dl/month) and the reciprocal of serum creatinine concentration ($1/S_{Cr}$) over time. The secondary end point will be to evaluate the percentage of patients who double S_{Cr}, progress towards dialytic therapy, or die during the study. Patients with nephrotic syndrome (serum albumin concentration <3 g%), systemic disease (including diabetes), severe cardiac or hepatic dysfunction, malignant or renovascular hypertension, obstructive nephropathy, initial serum potassium concentration >5.8 mmol/liter, will be excluded. After "wash out" period of four weeks, patients with arterial blood pressure ≥140/90 will be assigned either to fosinopril (10 to 30 mg/day) or nifedipine GITS (30 to 60 mg/day). In case of insufficient blood pressure control, Frusemide will be added in a first step and then atenolol and/or doxazosine in order to maintain arterial blood pressure control under 140/90. Patients with LDL-cholesterol ≥160 mg/dl will be treated with pravastatina. The relation between chronic renal failure progression and ambulatory blood pressure during 24 hours will be eventually studied.

Impact of rHu-EPO therapy on the quality of life in predialysis chronic renal failure (CRF) patients. *J.M. Lopez-Gomez, R. Jofre, F. Moreno, D. Sanz-Guajardo, F. Valderrabano, and the Spanish Cooperative Renal Patients Quality of Life Study Group.* The effect of rHu-EPO therapy on the quality of life (QL) and progressive decrease rate of renal function was evaluated in predialysis CRF. A total of 103 patients (72 treated with rHu-EPO and 31 untreated) were included in a multicenter, prospective and controlled study. The QL was assessed at baseline, and after 3 and 12 months using the Karnofsky Scale (KS) and the Sickness Impact Profile (SIP) questionnaire. A lower SIP score and higher KS score indicated a better QL. The impairment of renal function was evaluated with the slopes of the regression lines of 1/Cr and time, 12 months before and after the onset of the study. At baseline, there were no significant differences in age, gender, etiology of CRF, blood pressure and serum creatinine between both groups, but hematocrit (Htc) was lower in the treated group. At 3 months, Htc, KS and the three dimensions (physical, psychosocial and global) of the SIP were as follows:

	With rHu-EPO		No rHu-EPO	
	Baseline	3 Months	Baseline	3 Months
Htc %	24.8 ± 2.7	31.4 ± 5.0[a]	29.8 ± 4.2	28.9 ± 4.5
KS	66.6 ± 21.0	74.1 ± 12.4[a]	84.7 ± 13.9	82.5 ± 15.2
Physical	17.8 ± 17.3	12.5 ± 11.4[a]	7.4 ± 8.5	11.2 ± 16.7
Psychosoc	16.0 ± 13.1	12.6 ± 10.8[a]	19.7 ± 23.0	16.4 ± 17.2
Global	17.5 ± 12.0	14.2 ± 9.9[a]	12.2 ± 10.1	14.3 ± 14.1

Among those patients who were still with no dialysis therapy at 12 months, no significant changes in Htc or QL assessment were found compared with the 3 month data. The slopes of the regression lines of renal function before and after the beginning of the study in both groups did not show significant changes. In conclusion, the partial decrease of anemia in predialysis CRF patients treated with rHu-EPO results an improvement in QL. rHu-EPO in these patients does not result changes in the progression rate of renal function impairment.

Are the complementary tests (for localization and/or function) of the parathyroid glands in refractory hyperparathyroidism necessary before doing parathyroid surgery? *X. Cuevas, J. Sala, M. Fulquet, M. Chine, M. Ramirez de Arellano, I. Llado, O. Ibrik, J. Viladoms, C. Isamat, Nephrology, Surgery, Radiology, H. de Mollet, CTD. Hospital de Terrassa, Barcelona, Spain.* We wanted to know if complementary tests for localization and/or function of the parathyroid glands (PG) condition the decision about surgery. Thirteen complete surgical parathyroidectomies (PTx) were done with autotransplantation in 12 patients from a fragment of the PG into the opposite forearm of the AVF. The patients had refractory secondary hyperparathyroidism (sHPT) to the medical treatment [all received pulses of $1,25(OH)_2D_3$]. Twelve patients were in HD treatment and 1 in predialysis, 7♂/7♀, age 51.2 ± 12.5 years. HD time was 73.3 ± 46.1 months. Follow-up time post-PTx was 8.3 ± 7.7 months. By ultrasonography parathyroid (7.5 MHz) was realized on 13 patients, cervical CT scan on 9 patients and $^{99}Tc^{m}$ MIBI scan on 7 patients. Every PG was weighed on a precision scale (weight ≥ 0.005 g). All the PTx were effective, with presurgical i-PTH levels being 892 ± 417 (405–1840) pg/ml for 13 patients and post-surgical levels 130 ± 138 (6–396) pg/ml for 12 patients at 3 months, at 6 months 193 ± 127 (32–302) pg/ml for 6 patients, at 12 months 198 ± 127 (22–390) pg/ml for 4 patients. One patient had only 3 PG, 2 p. had 2 PG and the 10 remaining had the 4 PG removed. No ectopic PG were found. The total weight PG/patient was 4.35 ± 3.45 (0.79–11.48) g. The weight and localization of each PG was related to the complementary tests (ultrasonography, CT scan, $^{99}Tc^{m}$ MIBI), demonstrating that no test, either isolated or together with the others, conditioned the surgical decision nor the posterior evolution. For 8 patients with a post-operative time PTx 10.5 ± 3.1 (3–27) months, $^{99}Tc^{m}$ MIBI autotransplant and cervical were performed; there was no evidence of glandular activity in any patient despite showing an i-PTH of 173 ± 160 (6–390) pg/ml at the time of testing (in 4 patients the i-PTH levels were between 4 and 7 times higher than normal). In conclusion, (1) the complementary tests for localization and/or function of the hyperplastic parathyroid gland in refractory secondary hyperparathyroidism do not condition either the decision or the type of PTx surgery. (2) Further cases are needed to: (a) determine if it is necessary to continue these pre-surgical tests or if they should only be used to rule out hyperfunctioning ectopic parathyroid glands; and (b) determine the usefulness of the $^{99}Tc^{m}$ MIBI scan as a viable test.

Effect of desferrioxamine and deferiprone (L1) on bone cell MG-63 proliferation and on phosphatase alkaline activity. *M.L. Naves, M.A. Canteros, R. Elorriaga, E. Sánchez, J.B. Cannata, Bone and Mineral Research Unit, Instituto Reina Sofía de Investigación, Hospital Central de Asturias, Oviedo, Spain.* It has been demonstrated that chelators such as desferrioxamine (DFO) may interfere with cell proliferation. It is known that this effect likely applies also to bone. The aim of this work was: (a) to evaluate the effect of different concentrations of DFO and deferiprone on osteoblasts proliferation (MG-63) and to determine the possible role of iron on the proliferation and, (b) to analyze the effect of both chelators on the metabolic activity of these cells using the alkaline phosphatase activity as enzymatic marker of activity or cellular differentiation. The cell proliferation and the effect of the concomitant addition of iron were evaluated with different concentrations of DFO (1, 2, 5, 10, 20, 40 and 100 μM) and deferiprone (1, 2, 20, 100, 120, 150, 180, 200 and 300 μM) at 24 and 48 hours, while the phosphatase alkaline activity was studied at 24, 48 and 96 hours after the addition to the culture medium of DFO (20 and 100 μM) and deferiprone (150 and 300 μM). Cellular proliferation was

completely inhibited with 100 μM of desferrioxamine and 300 μM of deferiprone. In both cases this effect was corrected by means of coincubation with iron citrate. In the second phase, using the same doses that inhibited the bone cell proliferation, we did not observe an impairment in the production of the enzyme. On the contrary, according the time of incubation increases (96 hours), desferrioxamine and deferiprone at its higher dose (the same which inhibits bone cell proliferation) increased the alkaline phosphatase activity, reaching values even higher than those observed in the maximum values of controls. These results demonstrate that both desferrioxamine and deferiprone inhibit the proliferation of osteoblast-like cell line MG-63, and the effect seems to be related with the chelation of some fraction of available iron. In spite of the effect on bone cell proliferation, the chelators seem do not impair cellular activity.

Effect of the aluminum overload on PTH levels and PTH mRNA synthesis. *S. Barreto, C. Gómez, C. Díaz-Corte, A. Canteros, A. Hernández, J.B. Cannata, Bone and Mineral Research Unit, Instituto Reina Sofía de Investigación, Hospital Central de Asturias, Oviedo, Hospital Universitario de Canarias, Spain.* The inhibitory effect of aluminum (Al) on parathyroid function has been demonstrated clinically and experimentally. However, there are doubts still about the main mechanisms implicated. Does Al affect PTH synthesis or PTH release? The aim of this study was to evaluate the effect of different levels of Al overload on PTH levels and also in the glandular expression of PTH mRNA in rats with chronic renal failure (CRF). Nephrectomy (5/6) was performed in 36 male Wistar rats, aged three months, 441 ± 16 g of weight. After 5 weeks the rats were divided into three homogeneous groups according to the creatinine clearance: group I ($N = 11$) received Cl_3Al (32.5 mg/kg of Al), i.p. in two doses; group II ($N = 13$) received Cl_3Al (16.25 mg/kg of Al); group III ($N = 12$) received placebo. The animals were sacrificed two weeks later. PTH, serum and urine Ca, P, Cr and Al were performed before and after Al exposure. The parathyroid glands were removed, weighted and used to measure Al concentration and PTH mRNA. The levels of CRF, Ca and P were similar in the three groups. The weight of the parathyroid glands after the sacrifice was group I 0.86 ± 0.4 mg, group II 1.18 ± 0.7 mg, and group III 1.73 ± 0.25 mg ($P < 0.05$ between groups I and III). The overall PTH values increased 5 weeks after nephrectomy from 16.95 ± 13.44 to 24.33 ± 18.54 pg/ml, showing a significant decrease after the maximum Al overload in group I (24.46 ± 10.4 to 16.27 ± 7.8; $P < 0.01$). No differences were found in the other two groups. The mRNA expression was lower in group I (Mx Al overload). Serum Al was significant different between the three groups (group I 405.9 ± 85.6 μg/liter, group II: 184.2 ± 83.2 μg/liter and group III: 4.4 ± 1.8 μg/liter; $P < 0.01$), similar findings were observed in the Al and in the parathyroid glands (group I 132.3 ± 0.7, group II 21.4 ± 3, and group III 7.9 ± 2.1 μg/g; $P < 0.01$). The correlation between Al in parathyroid glands and in serum was significant, $r = 0.88$, $P < 0.05$. A reduction in glandular size, PTH levels and PTH mRNA expression was observed in the severe Al intoxication, suggesting that Al could have a direct action on PTH synthesis.

Mineral bone density variation in hemodialysis patients: Non-fractionated heparin (NFH) versus low molecular weight heparin (LMWH). *C. Bernis, A. García Vadillo, E. Muñoz de Bustillo, A. Fernández, A. Cirugeda, P. Sanz, E. Gruss, G. Barril, J.A. Sanchez Tomero, V. Alvarez, J.A. Traver, Nephrology and Rheumatology Departments, Hospital de la Princesa, Madrid, Spain.* Heparins inhibit type I collagen and DNA synthesis and can aggravate osteoporosis in hemodialysis (HD) patients. Some experimental data suggest that new LMWH induce less negative effects over bone formation than NFH. We studied 30 patients initiating HD, 23 of whom completed a 2 year follow-up. They were assigned to receive LWMH or NFH (13 and 10 patients, respectively). Both groups were similar according age (56 ± 14 vs. 61 ± 12; *P* NS), PTH levels (352 ± 132 vs. 262 ± 134; *P* NS) and both received similar doses of calcitriol (0.30 ± 0.3 vs. 0.5 ± 0.5; *P* NS). Bone mass at baseline and at two years was determined with a *Dexa Hologic QDR 1000* densitometer (variation coefficient 0.5%). Results are expressed in absolute values: bone mineral density g/cm^2 (BMD), BMD variation (var BMD), percentage of the peak bone mass of young normal sex-matched adults (PBM%), PBM% variation (var PBM%); or standard deviations from the mean of age and sex-matched normal Spanish subjects (Z-score) and Z-score variation (var Z score).

	NFH		
	Basal		24 months
BMD	0.862 ± 0.2		0.848 ± 0.2
var BMD		−0.013 ± 0.02[a]	
PBM%	81.6 ± 20.6		81.1 ± 20
var PBM%		−0.5 ± 2.4	
Z score	−0.63 ± 1.6		−0.73 ± 1.5
var Z score		−0.048 ± 0.11	

	LMWH		
	Basal		24 months
BMD	0.923 ± 0.1		0.927 ± 0.1
var BMD		+0.003 ± 0.2	
PBM%	88.2 ± 13		89.3 ± 13
var PBM%		+1.7 ± 3.4	
Z score	−0.73 ± 0.9		−0.57 ± 0.7
var Z score		+0.15 ± 0.3	

[a] $P < 0.1$

The group receiving NFH tend to lose more bone mineral density, showing a worsened Z score and BMP compared to the group assigned to LMWH, whose patients slightly improved those parameters. Further studies designed with more patients and for a longer time are needed to confirm these preliminary findings.

Modifications in the bone disease biochemical profile in patients transfered from hemodialysis (HD) to peritoneal dialysis (PD). *E. López Rubio, C. Gómez Roldán, L. Sánchez Tárraga, E. Gallego, J. Portolés, E. Olivas, F. Llamas, M. Orts, A. Serrano, E. Andrés, Division of Nephrology, Hospital General, Albacete, Spain.* Different types of bone disease in patients on dialysis have been observed. We evaluated possible changes in the biochemical profile of the bone disease of patients who changed dialysis therapy. We retrospectively researched 16 patients who changed from HD to PD and 5 from PD to HD. The analysis of urea, creatinine (Cr), calcium (Ca), ionic calcium (Ca++), phosphate (P), alkaline phosphatase (AP), intact PTH (iPTH), hematocrit (Hct), hemoglobin (Hb) and albumin (Alb), before the change, and after 3, 6 and 12 months under the new therapy. Results are analyzed by the paired data Student's *t*-test.

	Urea	Cr	Ca	Ca^{++}	P	AP	iPTH
3 months							
HD	144 ± 52	11 ± 2	9.2 ± 2	1.09	6.3	221	251
DP	116 ± 41[c]	11 ± 3	9.2 ± 2	1.17[a]	4.9[a]	311[a]	144[b]

	Hct	Hb	Alb
3 months			
HD	30.6	9.4	4
DP	37.2[b]	11.4[b]	3.5[b]

	Urea	Cr	Ca	Ca^{++}	P	FA	PTHi
6 months							
HD	143 ± 54	11.5 ± 2	9.1	1.09	6.5	227	268 ± 190
DP	123 ± 44	11.1 ± 3	9.2	1.16	4.8[a]	366[b]	253 ± 356

	Hct	Hb	Alb
6 months			
HD	31.2	9.5	4.1
DP	39.5 ± 9[c]	12.2[c]	3.8

[a] $P < 0.05$, [b] $P < 0.01$, [c] $P < 0.001$.

After 12 months with PD there were no significant differences except for the persistent correction of anemia. When they began PD, the mean KtV was 1.72 and NPCR was 0.86. The small number of patients transfered from PD to HD did not allow us to make adequate comparisons. In conclusion, (1) after 3 months with PD there is a decrease in iPTH. At the same time phosphate decreases and ionic calcium increases. (2) Eventually every parameter comes to the initial point. Among the possible causes, we consider that an increase in the dialysis dose that we provided with PD compared with HD over the previous weeks, as the most influential.

Lipid profile changes in our continuous ambulatory peritoneal dialysis population. *V. Pérez-Bañasco, P. Pérez del Barrio, F.J. Borrego-Utiel, M.V. Camacho-Reina, C. Sánchez-Perales, A. Liébana, S. García-Marcos, M.J. García-Cortés, J. Borrego-Hinojosa, P. Serrano, Servicios de Nefrologia y Bioquimica, Hospital General de Especialidades "Ciudad de Jaén," Jaén, Spain.* Changes in lipid profile are usual in patients with chronic renal failure who are on continuous ambulatory peritoneal dialysis (CAPD). We tried to analyze that profile in our patients on CAPD. This study included all of our patients on CAPD: 32 patients total, 13 males (41%) and 19 females (59%). Of them, 8 (25%) were diabetic, 24 (75%) were hypertensive patients and 12 (37.5%) obese. The average age was 59 ± 13 (28–82) years with 37 ± 44 (3–186) months on dialysis. None of them received hypolipidemic treatment during the two weeks to the prior to the inseption of this study.

	CAPD	Healthy controls	
	mg/dl		*P*
Total cholesterol	217 ± 53	160 ± 30	< 0.001
Triglycerides	180 ± 62	111 ± 20	< 0.001
HDL-chol	42 ± 8	60 ± 15	< 0.001
LDL-chol	138 ± 45	130 ± 39	NS
Apo Al	97 ± 12	135 ± 18	< 0.001
Apo B	97 ± 26	100 ± 15	NS
Lipo (a)	42 ± 22	20.5 ± 2.3	< 0.001
Albumin *g/dl*	3.8 ± 0.5		
Oncotic pressure	21 ± 22.5		

(1) Sex had influence on the level of HDL (male 37 ± 9 vs. female 44 ± 7 mg/dl, $P < 0.05$). (2) Age correlated with the value of albumin ($r = -0.50$, $P < 0.01$). (3) In the diabetic patients the level of albumin was lower (34 ± 6 vs 39 ± 4 g/liter, $P < 0.05$). (4) The hypertensive patients had higher levels of Apo B (102 ± 26 vs. 80 ± 19 mg/dl, $P < 0.05$). (5) In obese the triglycerides were higher (212 ± 66 vs. 161 ± 51 mg/dl, $P < 0.05$). (6) We found a correlation between total serum cholesterol and triglyceride levels ($r = 0.48$, $P < 0.01$), and between total serum cholesterol and Lipo (a) levels ($r = 0.36$, $P < 0.05$). (7) Also, a correlation exists between triglycerides and HDL-chol levels ($r = -0.49$, $P < 0.01$), triglycerides and LDL-chol levels ($r = 0.38$, $P < 0.05$), and triglycerides and Apo B levels ($r = 0.51$, $P < 0.05$). (8) Also, we found a correlation between LDL-chol and the Lipo (a) levels ($r = 0.38$, $P < 0.05$). (9) We didn't find a correlation between lipid levels and oncotic pressure, and between lipid levels and the load of glucose (daily intraperitoneal dose of glucose). We conclude that: (1) the lipid profile is significantly altered in the patients on CAPD. (2) Lipo (a) is the most modified parameter. (3) The load of intraperitoneal glucose doesn't seem to influence the lipid parameters.

Mortality in a multicenter registry of peritoneal dialysis. *C. Gómez Roldán, A. Miguel, R. Garcia, J. Alvariño, M. Lanuza, R. López, J. Pérez Contreras, F. Tornero, J. Olivares, Multicenter Study Group on Peritoneal Dialysis from Albacete, Cuenca and Autonomic Communities of Valencia and Murcia, Spain.* From 1992 our work group has carried out a registry of patients with chronic renal failure on peritoneal dialysis (PD). As of December 31, 1995 there were 526 patients. Between January 1, 1992 and December 31, 1995 there were 111 deaths (21%) and they are the study objective; 53 (47.7%) were women and 58 (52.3%) were men. The mean age was 65.5 ± 10.6 years when they began the technique, and mean permanence on PD was 30.74 ± 24.25 months (range 1.6–106.7). There were 28 (25.2%) patients who spent less than one year on PD, 45 between 1 and 3 years, 23 between 3 and 5 years and 15 (13.5%) for more than 5 years. The mean weekly Kt/V was 1.86 ± 0.48 and the mean PCRN was 0.97 ± 0.37 (measured in 28 patients only). Death was due to cardiovascular disease (16, 14.4%); cerebrovascular disease (14, 12.6%); infection (21, 18.9%); peritonitis (5, 4.5%); withdrawal from dialysis (5, 4.5%); other causes (22, 19.8%) and in 28 (25.2%) the cause was unknown. Between 1993 and 1995 there were 79 patients alive. There were 68 peritonitis episodes in 42 patients (one case of peritonitis in 30 patients, two peritonitis in 3 patients and three or more in 9 patients). There were 27 admissions for peritonitis; admission duration was 11.4 ± 12.8 days/3 years. There were 148 admissions (other causes) in 67 patients. Admission duration was 11.6 ± 11.3 days, and 21.7 days per patient/3 years. There were 28 patients, 16 men and 12 women, on PD for less than one year. The mean age was 63.8 ± 13 years (range 33–83), mean permanence was 5.73 ± 3 months, mean weekly Kt/V was 2.39, and mean PCRN was 0.93. Death was due to cardiovascular disease (14.2%), cerebrovascular disease (21.4%), infection (21.4%), peritonitis (7.1%), withdrawal from dialysis (3.5%), other causes (18.2%), and in 14.2% the cause of death was unknown. There were 13 admissions (5.85 days per patient during 3 years). There were 15 patients, 9 women and 6 men, on PD for more than 5 years. The mean age was 64 ± 8.7 years, mean duration was 75.9 months, mean weekly Kt/V was 1.76, and mean PCRN was 1.01. Death was due to cardiovascular disease (6.6%), cerebrovascular disease (13.3%), infection (13.3%), peritonitis (13.3%), withdrawal from dialysis (20%), and in 33.3% the cause was unknown. There were 21 hospitalizations of 8.76 days (12.26 days per patient during 3 years). In conclusion, (1) 21% of the patients included in the study died during 4 years (5%/year). (2) The mean permanence on PD of this group is slightly less than all the patients enrolled. (3) The most frequent causes of death were unknown, vascular and infectious diseases. (4) Withdrawal from dialysis is a very significant cause of death. (5) Hospital admission was higher in patients with longer tenures on PD.

Short term evolution of the residual renal function in patients in continuous ambulatory peritoneal dialysis. *R. López-Menchero, A. Miguel, R. Garcia Ramón, Department of Nephrology, University Clinical Hospital of Valencia, Spain.* Residual renal function is a fundamental factor to obtain indicators of optimum for doses of dialysis as well as nutritional status. The purpose of the study was (1) to study the evolution of the residual renal function in patients in continuous ambulatory peritoneal dialysis (CAPD) in the first months of treatment, and (2) to evaluate this evolution with the residual clearance at the beginning of the treatment. We studied the evolution of the residual renal function (RRF, average of the clearances of urea and creatinine) in 24 patient on CAPD for a minimum of 12 months of treatment (16 male and 8 women, mean age 55.1 ± 17.3 years). We measured the dose of dialysis (peritoneal and renal Kt/V) and the nPCR (formulation of Ronco). The values are expressed as mean ± SE, and the comparisons between variables were accomplished through nonparametric methods (Mann-Whitney and Friedman). The global results were the following:

	Month 1	Month 6	Month 12	*P*
RRF *ml/min*	6.19 ± 3.33	5.36 ± 3.38	4.28 ± 3.25	< 0.01
Kt/V *weekly*	2.42 ± 0.54	2.35 ± 0.53	2.18 ± 0.54	< 0.01
nPCR *g/kg/day*	1.11 ± 0.30	1.13 ± 0.32	1.03 ± 0.30	= 0.05

The data of 14 patients to 18 months are: RRF 3.65 ± 4.18 ml/min; weekly Kt/V 2.04 ± 0.47; nPCR 0.97 ± 0.20 g/kg/day. Three (12.5%) patients had lost their renal function at 12 months, and 5 of 14 studied to 18 months (35.7%). This evolution with the residual clearance at the beginning of the treatment was also studied (group A, RRF < 5.45 ml/min, $N = 12$; group B, RRF > 5.45 ml/min, $N = 12$).

	Age *years*	RRF	KtV	nPCR
Month 1				
Group A	60.2 ± 18.4	4.02 ± 1.24	2.23 ± 0.44	1.00 ± 0.32
Group B	49.9 ± 15.1	8.36 ± 3.37	2.61 ± 0.57	1.22 ± 0.32
P	NS ($P = 0.1$)	< 0.01	$= 0.05$	NS ($P = 0.1$)
Month 12				
Group A		2.61 ± 2.31	1.93 ± 0.36	0.83 ± 0.10
Group B		5.95 ± 3.26	2.42 ± 0.59	1.23 ± 0.30
P		<0.05	$= 0.05$	< 0.001

After 1 year 3 patients who had completely lost the RRF were in group A. In conclusion (1) the patients on CAPD maintain a high percentage of the initial residual renal function during the short term. (2) The precocious beginning of the dialysis, with its important residual renal function, allows the nephrologist to maintain the patient's optimum dialysis dose and nutritional status during the course of treatment.

Supraventricular arrhythmias (SVA) in hemodialysis (HD). *E. Verde, A. Pérez de Prado, M.C. Vozmediano, R. Pérez, R. Jofré, J.M. López, E. Junco, J. Almendral, J. Osende, F. Valderrábano, Department of Nephrology and Cardiology, Hospital General "Gregorio Marañón," Madrid, Spain.* Supraventricular arrhythmias (SVA) have been poorly characterized in HD patients (pts). The aim of the present study was to analyze the incidence and type of SVA and premature atrial contractions (PAC) in HD. Eighty-two pts in sinus rhythm (44 M/38 F; mean age 58 ± 13 years) were studied with ECG-Holter monitoring during 6 consecutive sessions of HD (mean time 15.9 ± 2.5 hours). Hemodiafiltration was used in 8 pts. M-mode and 2-D echocardiograms were performed on a non-dialysis day. The prevalence of hypertension and diabetes were 68% and 26%, respectively, and 26 pts had ischemic heart disease. The total incidence of SVA was 46.3%. Supraventricular tachycardia was the most frequent SVA (33 pts), followed by atrial flutter (6 pts) and finally atrial fibrillation (3 pts). Moreover, PAC of significative density (>1 PAC/1,000 beats) were documented in 51% of the pts. SVA and PAC were recorded mostly in the last hours of HD. This feature correlated to lower potassium and ionic calcium serum levels. Non-sustained-SVA were recorded in hemodiafiltration patients. The echocardiograms showed a high prevalence of left ventricular hypertrophy (72%) and left atrial dilation (87%). Right atrial dilation (34%) was correlated with a high incidence of SVA and PAC. Conversely, left ventricular hypertrophy was not associated with SVA. In conclusion, HD pts have a high incidence of SVA, especially in the last hours. This feature could be associated with electrolytic changes during dialysis. Pts treated with hemodiafiltration have a decreased incidence of SVA. Right atrial dilation could be a risk factor for SVA.

Nerve conduction speed (NCS) as a method for monitoring suitable dialysis over 5 years. *J.L. Lerma, T. López-Alburquerque, J.L. Sánchez Rodríguez, B. Martín, J. Diego, J.M. Tabernero, Servicios de Nefrología y Neurología, Hospital Universitario, Salamanca, Spain.* NCS is a test periodically implemented to assess the suitability of the amount and quality of dialysis. However, few recent works have addressed its usefulness in series or its repercussions in dialysis. This study was designed to (1) correlate neurological exploration and NCS; (2) to determine the correlation between NCS, suitable dialysis parameters and the type and duration of HD; (3) to assess the influence of NMS on treatment (dose of HD, change of membrane). Seventy-six patients on HD and 3 on CAPD were studied (51 men, 28 women, with a mean age of 59.9 ± 14.9 years over five years). Subjects were divided into 2 groups: (1) with diabetes mellitus (DM) $N = 15$; (2) without DM, $N = 64$. Serial electrophysiological studies were performed annually; these consisted of measuring NCS, amplitude, and the mean latency time of the common peroneal nerve. At the same time, neurological assessments were made for Kt/V, PCR, TAC. Statistical significance was evaluated with ANOVA and correlation and simple linear regression studies, comparing the evolution of NCS over time with the different parameters studied. We found that (1) no significant variations were observed over time in the neurophysiological parameters analyzed [mean latency time, motor conduction speed (MCS) amplitude]; (2) patients with clinical signs of polyneuropathy Achilean areflexia at the start of the study displayed a significantly reduced MCS (40.9, $N = 56$ *vs.* 37.8, $N = 23$, $P < 0.03$); (3) of the 35 patients with MCS < 40 in the first study, 23 continued with the same time and dialysis membrane in the second study and in 14 the MCS became normalized or improved; (4) of the 15 diabetics, only 4 had normal MCS values at the start of the study; (5) the women ($N = 27$) had significantly greater MCS values than the mean ($N = 52$) (41.9 *vs.* 39.1, $P < 0.04$); (6) the patients dialyzed with PAN ($N = 17$) had greater MCS values than those dialyzed with cuprophane ($N = 59$), although statistical significance was not reached (41.6 *vs.* 39.9; NS); (7) there was no correlation between the MCS and KtV ($P < 0.55$). In conclusion, we determined that (1) Achilean areflexia was the exploratory finding that best correlated with the reduction in MCS; (2) there were no significant differences between the patients dialyzed with cuprophane and polyacrylonitrile, nor between KtV and MCS; (3) in the group with DM, MCS deteriorated progressively and was not suitable as a marker of suitable dialysis; (4) MCS was considered to be a complementary datum and few therapeutic decisions were made based exclusively on its assessment; (5) currently, there are simpler, more accurate and more reproducible ways of assessing suitable dialysis.

Efficacy of the therapy to eradicate *Helicobacter pylori* in dialysis patients evaluated by C13 urea breath test and serology. *E. Muñoz de Bustillo, J.A. Sánchez-Tomero, J.C. Sanz, A. Fernández, A. Cirugeda, V. Alvarez, G. Barril, C. Bernis, J.A. Moreno, I. Jimenez, M. López-Brea, J.A. Traver, Nephrology, Microbiology, and Gastroenterology Departments, Hospital Universitario de la Princesa, Universidad Autónoma, Madrid, Spain.* The prevalence of *Helicobacter pylori* (HP) infection in our unit reachs a 62%. It is well known that certain therapies that eradicate this infection prevent the development of peptic ulcer, but there is limited information concerning the application of this therapies to hemodialysis (HD) patients. In order to assess the efficacy of this therapeutical regimen, we studied 34 HD patients prospectively during 18 months, determining HP infection through C13 urea breath test (UBT). The patients' mean age was 63 ± 10.6 years, 16 were female and 18 male. Those positive patients referring with dispepsia, antecedents of peptic ulcer or who were included in the transplantation list were treated with amoxicillin, 500 mg/8 hr and omeprazol 20 mg/12 hr for two weeks. At six months the UBT was repeated, and those patients who were still positive received chlaritromicin 250 mg/12 hr plus Omeprazol 20 mg/12 hr. In addition, 24 patients were evaluated with serology (*Ig piloriset Diagnostica*) at months 0, 6 and 18. In this group 24 of 34 patients included were positive with UBT; 16 of them were treated with the first therapeutic regimen, and 8 became negative. The rest received the second regimen, and 5 more responded. Thus, after both regimens, HP infection was eradicated in 88.5% of patients, with extremely good tolerance. Only one patient negative at beginning of the study acquired the infection during the study period. One positive patient who was not treated became negative spontaneously. Regarding serology, no changes were observed in those 9 patients with negative UBT who were still negative at 18 months, nor in those 5 positive untreated. The patient who became positive raised his titration (+66%). In 10 patients successfully treated, the antibody titration decreased only 8.8% at 6 months (from 2424 ± 3522 to 2612 ± 2796; P = NS), but was at 63.6% at 18 months (to 638 ± 619; $P < 0.001$). The response of HP infection to amoxicillin or chlaritromicin plus omeprazol is satisfying and well tolerated. Even when it is difficult to diagnose the infection by serology because the cut-off is difficult to determine, the evolution of the antibody titration at 18 months, but not at 6, could be useful to evaluate the response to treatment in those centers that lack the spectrophotometer needed to perform the C13 UBT.

Echocardiographic findings in patients with episodes of hypotension in hemodialysis. *M. Ruiz-Nodar, A. Cirugeda, C. Bernis, J. Enero, E. Iturralde, G. Barril, J.A. Traver, Departments of Nephrology and Cardiology, University Hospital of La Princesa, Madrid, Spain.* Intradialytic hypotensive episodes are a serious problem that increases in elderly patients. Echocardiography may be a valuable tool for the diagnosis and treatment. Left ventricular hypertrophy (LVH) has a high frequency and is an important determinant of survival, more so than coronary artery disease. It is also more amenable to therapeutic intervention. Of 70 patients in our hemodialysis unit, we performed an echocardigraphic study involving the 21 patients with episodes of hypotension. All used a bicarbonate-containing dialysis solution. Mean age 67.3 years (SE ± 10.5); 62% male; 57% hypertension and 14% diabetic. Mean time on dialysis 43.7 months. A total of 29% had ischemic cardiac disease (19% acute myocardial infarction and 10% angina pectoris), and 9% atrial fibrillation. The etiology of end-stage renal disease was: 24% chronic pyelonephritis, 19% nephrosclerosis, 14% glomerulonephritis, 9% diabetic nephropathy, 5% systemic diseases, 5%

polycystic renal and 24% unknown. The study showed the following echocardiographic findings: 52% left atrium dilation; 62% degenerative valvular changes; reduction in ejection fraction and LVH (Table 1); septum thickness 14.4 mm ± 2.8 ($N < 11$); posterior wall thickness 13.6 mm ± 2.8 ($N < 11$). Doppler echocardiographic showed a reduction of ventricular relaxation of 57%, restrictive patter by ventricular stiffness 5%, and normal was 38%. This study showed diastolic dysfunction in 58% and systolic dysfunction in 19%.

	Light	Moderate	Severe	Normal
Reduction ejection fraction	5%	9.5%	9.5%	76%
LVH	9.5%	33.5%	38%	19%

Most patients with hypotensive episodes during dialysis show diastolic dysfunction in LV, and diastolic failure by LVH is the most important cause. The echocardiographic study in these patients is very important for the maintenance and treatment while they are on hemodialysis treatment.

Quality of life (QL) in diabetic dialysis patients: A Spanish cooperative study. *Spanish Cooperative Renal Patients Quality of Life Study Group. Coordinators: F. Moreno, D. Sanz-Guajardo, J.M. Lopez, R. Jofre, F. Valderrábano, Hospital Príncipe de Asturias, Hospital Puerta de Hierro, Hospital General Universitario Gregorio Marañón, Madrid, Spain.* At the present moment, 18% of the patients starting renal replacement therapy in Europe are diabetic. In this study, the QL of 1,023 stable patients on chronic dialysis, selected randomly on a national level, was evaluated. The evaluation of QL was done by the Karnofsky Scale (KS) and the Sickness Impact Profile (SIP). A lower KS score and a higher SIP score indicated a lower QL. Comorbidity was evaluated by the Friedman Comorbidity Index (CI). Eight percent of the patients studied were diabetic ($N = 82$); 17% were on DPA and 83% on hemodialysis. Of these, 65% used bicarbonate dialysis and 37% used synthetic membranes. Twenty percent were blind and 37% showed intermittent claudication. Principal comorbidity factors were the loss of vision, hypertension, osteomuscular-locomotive and gastrointestinal pathologies and cardiac insufficiency. The mean age and CI of the diabetics (D) were higher than those of the non-diabetics (ND) (mean ± SD; age, D 56 ± 13 vs. ND 53 ± 15, $P < 0.05$; CI, D 6.4 ± 3 vs. ND 4.5 ± 3, $P < 0.0001$). There were no differences in hemoglobin level, Kt/V or PCR. The diabetic patients showed lower scores on all the global QL indicators used [median and 25, 75 percentiles; KS, D 60 (50, 70) vs. ND 80 (60, 90); SIP Physical Dimension, D 18 (6, 32) vs. ND 6.5 (2, 15); SIP Psycho-Social Dimension, D 17 (8, 28) vs. ND 9.3 (4, 19); Global SIP, D 20 (11, 32) vs. ND 11 (6, 20)]. The differences persisted after adjusting the scores to differences in age, sex, hemoglobin, educational level and socio-economic level ($P < 0.001$ in all). After including the adjustment of the CI covariables blindness and intermittent claudication, the differences between D and ND were reduced, although significant differences in the SIP Physical Dimension ($P < 0.05$) and KS ($P < 0.001$) were maintained. In conclusion, diabetic patients on dialysis show severe limitations in independence and functional state. The comorbidity related to diabetes plays a crucial role in the deterioration of their quality of life.

Factors related to the quality of life (QL) of ESRD patients on dialysis. *F. Moreno, D. Sanz-Guajardo, J.M. López, R. Jofre, F. Valderrábano, on behalf of the Cooperative Spanish QL Study Group.* We evaluated 1023 patients on dialysis, randomly selected from among 42 hospitals and their extrahospitalary dialysis clinics. The criteria for selection were: over 15 years of age; a minimum of three months on the same therapy; three months since the last major complication; if they received EPO, at least three months of treatment; absence of vascular access problems. The evaluation of QL was done on the Karnofsky Scale (KS) and the Sickness Impact Profile (SIP), both self reported. The SIP items were grouped to obtain a Physical Dimension, a Psychosocial D, and a Global Score SIP. Comorbidity was measured on the Friedman Index (CI). A multivariate analysis through stepwise linear regression was carried out. Among the independent variables included were personal characteristics, socio-economic and cultural levels, CI, type of substitute therapy, hemoglobin, Kt/V, PCR, previous unsuccessful transplant, time on dialysis, type of dialysis center, type of dialyzer membrane and dialysis solution, and treatment with EPO. Factors related negatively to QL according to the Physical D and the Global Score of the SIP were: first, the CI and age, and second, the presence of diabetes and the female sex. Factors related to a better QL according to the same indicators include level of studies, socio-economic level, and higher level of hemoglobin (R^2 Ln Global SIP, 0.28; R^2 Ln Physical D, 0.34). The KS factors related to a lower QL were age, CI, the presence of diabetes and blindness. A higher socio-econimic level and a higher level of studies were related to a better score on the KS (R^2 Ln KS: 0.31). Kt/V, dialysis technique and type of dializer membrane or dialysis solution showed no relation to QL in this study. Comorbidity and age are the factors most strongly related to a lower QL in dialysis patients. A higher cultural and economic level and a higher hemoglobin level are related to better QL.

Quality of life in dialysis patients. Spanish national study on quality of life in dialysis. *F. Moreno, J.M. López, D. Sanz-Guajardo, R. Jofre, F. Valderrábano, on behalf of the Cooperative Spanish QL Study Group (CSQLSG).* The objective of this study was to evaluate the QL in patients on chronic dialysis. The transversal study was carried out nationally and 1023 patients on dialysis, randomly selected from among 42 hospitals and their extrahospitalary dialysis clinics, were evaluated. The criteria for selection were: (1) age >15; (2) at least 3 months on the same therapy; (3) 3 months since the last major complication; (4) if on EPO, at least 3 months of treatment; (5) absence of vascular access problems. The evaluation of QL was done through the Karnofsky Scale (KS) and the Sickness Impact Profile (SIP), all were self-reported. The SIP evaluates illness-related behavioral dysfunction and includes a Physical Dimension, a Psychosocial D and a Global Score; a higher score indicated a lower QL. The mean age was 53 ± 15; 41% were ≥60 years old; sex, 56% M and 44% F; 8% were diabetic; 88% were on hemodialysis (HD) in center, 0.7% on home HD, 7% on hemodialfiltration and 4% on DPA; 73% received EPO. The average hematocrit (Ht) was 30% and 12% had Ht lower than 25%. The results of the QL indicators are the following (the median and the 25 and 75 percentiles are shown): KS, 70 (60–90); Physical D, 7 (2–17); Psychosocial D, 10 (4–20); Global Score of the SIP, 12 (6–21). A total of 26% of the patients scored ≥20 on the SIP Global Score and 31% <60 on the KS. No significative influence was found relating to dialysis technique, dialysis solution (acetate vs. bicarbonate), nor the use of a synthetic or cellulose dialyzer membrane. Twenty-six percent of the patients in this study showed an important adverse effect of the disease on their QL (SIP Global Score ≥20). No differences on QL were found among patients with different renal substitutive therapeutic modalities, nor in the type of dialyzer membrane or dialysis solution.

Renal replacement therapy with hemodialysis in patients over 65 years of age. *M.C. Sánchez Perales, M.J. García Cortes, F.J. Borrego Utiel, A. Liebana Cañada, J. Borrego Hinojosa, S. García Marcos, P. Serrano Angeles, V. Pérez Bañasco, Servicio de Nefrologia, Hospital General de Especialidades, Jaén, Spain.* A greater life expectancy in general population and improvements in dialysis techniques are providing more acceptance of elderly patients in dialysis programs. The aim of present study was to evaluate potential differences in epidemiologic data, morbidity, survival as well as biochemical parameters that have been reported to correlate with nutritional status and morbidity such as hemoglobin (Hb), creatinine (Cr), urea and serum albumin (Ab) in patients older 65 years included on hemodialysis. We studied the population included on hemodialysis from January 1988 to December 1994. Patients who had undergone prior transplantation, transferred from other dialysis facilities or from other forms of dialysis were excluded. Follow-up began at the start of hemodialysis and ended on transplantation, death, transferring to other center, change in dialysis modality or closing of the study on December 1995. We analyzed differences among patients below or above 65 years about follow-up at our center prior to starting dialysis, cause of end-stage renal disease, concomitant and intercurrent diseases as well as survival and hospitalization as the index of morbidity. Biochemical parameters were evaluated at start of hemodialysis and final of follow-up. We examined the relationship between morbidity and baseline biochemical parameters. A total of 157 patients had been included on hemodialysis and 28% ($N = 44$) of them were older 65 years at the start of treatment. Their inclusion

increased from 8.5% in 1988 to 45.7% in 1994. We found statistically significant differences in the elderly patients: (1) They were referred to our center in very advanced stage of chronic renal failure (59% vs. 37% of younger patients, $P < 0.05$; (2) A higher frequency of hypertensive nephrosclerosis in etiology of end-stage renal disease (23% vs. 5%) as well as cardiovascular comorbid conditions (27% vs. 8%) $P < 0.01$ (3) Baseline serum albumin (g/dl) was 3.86 ± 0.64 vs. 4.21 ± 0.53, $P < 0.001$; final, 4.17 ± 0.52 vs. 4.47 ± 0.48, $P < 0.01$; baseline creatinine (mg/dl), 9.08 ± 1.87 vs. 10.22 ± 2.20, $P < 0.01$ final, 8.77 ± 1.5 vs. 10.41 ± 2.27, $P < 0.001$. (4) More intercurrent diseases (86% vs. 62%, $P < 0.01$) due to infection and cardiovascular causes and higher use of permanent catheter for vascular access (24% vs. 5%, $P < 0.01$). (5) Greater number of hospital admissions per year: 2.95 ± 3.40 versus 1.67 ± 2.02, $P < 0.05$. (6) Baseline levels of Hb, Urea and Cr did not correlate with hospitalization rate. By multivariate linear regression analysis, morbidity correlated inversely with initial serum Albumin and directly with age at the start of dialysis ($r = 0.47$; $P < 0.001$). (7) Lower survival rate. At 1 year, 79.48%, 5-years, 52.77% versus 1 year 95.32%, 5 years 84.94% (Log-rank test: $P < 0.001$). In summary, hemodialysis patients older than 65 years at the start of treatment were found to have: (1) increased acceptance in the hemodialysis program; (2) late referral to our Nephrolgy Unit; (3) more vascular and cardiac disease that increases morbidity and disables to get a vascular access; (4) lower initial serum albumin as a nutritional marker associated with increased risk of morbidity.

Valvular heart calcification on chronic hemodialysis patients: Prevalence and related factors. *M. Salgueira, O. Jarava, V. Martí, A. Monroy, N. Aresté, R. Moreno Alba, J.A. Milán, Nephrology & Cardiology Services, Hospital Universitario Virgen Macarena, Seville, Spain.* Valvular heart calcification (VC) appear frequently and prematurely in patients (pts) who have been receiving maintenance hemodialysis (HD). The etiologic factors are: aging, dialysis duration, metabolic and hemodynamic factors. We wanted to identify valvular disease in our pts on chronic HD and evaluate the role of different related factors. Seventy unselected pts (38 M/32 F, aged: 50 ± 15 years, dialysis duration, 86 ± 62 months). Serum level of total and bone alkaline phosphatase (TAP, BAP), BGP, iPTH, calcium and phosphorus had been measured for the three preceding years. M-mode, two dimensional and Doppler echocardiography was performed in all pts. We stratified the pts according to age (><60 years) and treatment duration (><72 months). The results showed (1) valvular heart disease, mitral stenosis (4%) and insufficiency (22%); aortic stenosis (11%) and insufficiency (10%). (2) Valvular heart calcification were seen in 28 pts (40%): aortic valve 10%, mitral valve 54%, and both 36%. (3) Pts with valvular calcification (VC+) were older ($P < 0.01$) and showed more peripheral vascular calcification ($P < 0.0001$) compared with VC− pts. Sex, arterial pressure, diabetes or cardiac output were not differents in both groups. (4) Pts VC+ younger than 60 were on HD for a longer time ($P < 0.05$). (5) Ca-P product were significantly higher in VC+ pts older than 60. (6) Mitral annular calcification didn't show a stadistical relationship with any biochemical marker of osteodystrophy. (7) Pts younger than 60 with aortic annular calcification showed higher PTH ($P < 0.05$), TAP and BAP (P = NS). In conclusion, (1) In the incidence of VC among our dialysis patients is high (40%), and mitral annular calcification is the most frequent. (2) Age and dialysis duration (mainly in younger patients) seem to play a role in the development of VC. (3) Abnormal calcium-phosphorus metabolism doesn't show up as an important factor related to our patients.

State of adrenergic system and renin-angiotensin system in chronic hypotension associated to uremia. *N. Esforzado, A. Cases, M. Bono, J. López-Pedret, L. Revert, A. Darnell, Nephrology Unit, Hospital Clinic i Provincial, Barcelona, Spain.* To study the pathophysiology of chronic hypotension (CH) in uremic patients, the state of adrenoceptors and of the renin-angiotensin system (RAS) in ESRD hemodialyzed patients were evaluated. Plasma catecholamine levels, plasma angiotensin II levels (Ang II_p), plasma renin activity (PRA) and α_2-(α_2A) and β_2-(β_2A) adrenoceptor density were measured, in 14 normotensive hemodialysis (HD) patients (NHC), 14 chronic hypotensive HD (HHP) patients and 17 normotensive control subjects. Plasma catecholamine levels were elevated in both HD groups ($P < 0.01$ vs. controls). Epinephrine levels were higher in chronic HHP ($P < 0.05$ vs. normotensive HD patients). PRA and Ang II_p were elevated only in chronic HHP patients ($P < 0.05$ vs. normotensive HD patients and controls). α_2A and G_2A densities were lower in HHP than in normotensive HD patients ($P < 0.05$). In all HD patients, mean blood pressure (MBP) correlated with α_2A ($r = 0.46$, $P < 0.01$) and G_2A ($r = 0.43$, $P < 0.05$) density. In HD patients, MBP also correlated with PRA ($r = -0.59$, $P < 0.01$) and Ang II_p ($r = -0.80$, $P < 0.01$). In a hypotensive HD subgroup of 10 patients, plasma epinephrine levels were very high ($P < 0.01$ vs. normotensive patients), whereas the PRA and Ang II_p were within the normal range (no differences vs. normotensive patients). In the hypotensive HD subgroup ($N = 4$ patients) plasma epinephrine levels were similar to normotensive HD patients, whereas the PRA and Ang II_p were very elevated ($P < 0.01$ vs. normotensive patients). Finally, plasma epinephrine levels were inversely correlated with PRA ($r = -0.78$, $P < 0.01$) and with Ang II_p ($r = -0.66$, $P < 0.05$) only in the hypotensive HD group. Although the adrenergic system impairment seems to be the main etiopathogenic mechanism of chronic hypotension in hemodialyzed patients, a renin-angiotensin system alteration could also be important in a small subgroup of hypotensive hemodialyzed patients.

Doppler spectrum analysis of the lower limb arteries and risk factors for atherosclerosis in patients on dialysis. *A. Tato, J. Pascual, F.J. Burgos, V. Gómez, T. Cano, G.F. Juárez, L. Orofino, F. Liaño, J. Ortuño, Servicios de Nefrología y Urología, Hospital Ramón y Cajal, Madrid, Spain.* The prevalence of atheromatosis of major arteries and associated morbidity and mortality in ESRD patients is very high, and constitutes the most important issue for the evaluation of a potential renal allograft recipient. It is not known whether Doppler spectrum analysis of lower limb arteries is useful in this evaluation. The correlation between vascular risk factors and this analysis is also unknown. Fifty-one dialysis (95.3% hemodialysis) patients underwent a Doppler ultrasound spectrum analysis of lower limb arteries (femoral, popliteal and posterior tibial). Mean age was 42 ± 5 years and time on dialysis 34 ± 6 months; 84% were hypertensive taking drugs; 47% were smokers (27 ± 4 cig/day during 162 ± 54 months). Acceleration (AC), mean velocity (MV), peak systolic (MxSV) and minimal diastolic (MnDV) velocities, pulsatility (PI) and resistance index (RI) were measured. RI and PI were maximal, and MxSR, MV and AC were minimal at the popliteal level. The number of cig/day was inversely correlated with perfusion parameters at popliteal and posterotibial arteries ($r = -0.78$ for PSR, -0.77 for AC and -0.68 for MnDR, all $P < 0.05$). Cholesterol levels were inversely correlated with posterotibial MV (r = -0.43). Systolic and diastolic BP and time of hypertension were directly related with RI at the femoral artery ($r = 0.38/0.43$). Fifteen patients received cadaveric transplantation. RI at the popliteal and posterior tibial arteries increased (1.5 vs. 1.7 and 1.2 vs. 1.6), as a result of significant reductions of perfusion velocities (popliteal, MV 4.1 vs. 0.2 and MxSV 28.7 vs. 23.4; post.tibial, MV 6.2 vs. 0.2 and MxSV 32.6 vs. 15.2 cm/sc). Doppler spectrum analysis of the lower limb arteries is a useful tool for the evaluation of the vascular situation of patients on dialysis. This technique could be useful in interventional pharmacological studies in this high risk population, and in the evaluation of these anastomosis without a high risk of further claudication.

Hypercatabolism induced by dialysis session and urea nitrogen generation: Effect of different dialysis membranes. *C. García Cantón, R. Palomar, A. Moreno, A. Toledo, S. Suria, P. Rossique, N. Esparza, M.D. Checa, Servicio de Nefrología, Hospital Insular de Gran Canaria, Spain.* It is known that the hemodialysis procedure can produce a hypercatabolic stimulus that could increase urea nitrogen generation on dialysis days, and this effect can be affected by the biocompatibility of the membrane used. Our aim was to compare the rate of urea generation on a group of patients on dialysis days and non-dialysis days, studying the influence of the type of dialysis membrane used. We prospectively studied two groups of 20 stable chronic hemodialysis patients. Group I, 12 males, 8 females, average age 49 ± 18, mean duration on dialysis 22 ± 27 months were studied for two weeks using cuprophane dialyzers in the first week and then AN69 dialyzers, maintaining the other dialysis parameters unchanged. Group II, 13 males, 7 females, average age 49.9 ± 14, mean duration on dialysis 16 ± 17 months were dialyzed with cellulose diacetate one week and poliamida dialyzers the other week. During each week of treatment the time between

the second and the third dialysis sessions was divided into two different periods: period I includes the first 22 hours postdialysis after urea rebound and period II the rest of the time until the next dialysis. The rate of urea generation was calculated in both periods for each membrane used.

	Bun generation period I mg/min	Bun generation period II mg/min	P
Group 1			
Cuprophane	6.63 ± 2	4.4 ± 2	< 0.001
AN69	5.3 ± 1.6	4.2 ± 2	< 0.05
Group 2			
Cellulose diacetate	7.2 ± 1.8	4.6 ± 2	< 0.001
Poliamida	6.3 ± 1.7	5.1 ± 2	< 0.05

A nonstatistical significant difference was observed in a weak urea nitrogen extraction between the different membranes. We calculated the difference between the rate of urea generation in period I and period II that was significatively higher with the less biocompatible membranes: cuprophane 2.49 ± 17 vs. AN69 1.04 ± 1.9; $P < 0.01$; cellulose diacetate 2.6 ± 1.7 vs. poliamida 1.08 ± 1.4; $P < 0.005$. There was no difference in the protein intake measured by dietetic register between period I and period II. Our results suggest that the rate of urea generation is higher in the period immediately postdialysis than in the rest of the interdialysis period, probably because of the catabolic stimulus induced by dialysis, and this was higher with cuprophane and cellulose diacetate than with AN69 and poliamida, suggesting a more hypercatabolic stimulus with the less biocompatible membrane.

Lipoprotein (a) reduction in dialysis patients after androgen therapy. *J.L. Teruel, M.A. Lasunción, A. Tato, T. Tenorio, M.E. Rivera, A. Aquilera, R. Marcén, J. Ortuño, Department of Nephrology and Biochemistry-Research, Hospital Ramón y Cajal, Madrid, Spain.* Lipoprotein (a) [Lp(a)], is currently regarded as an independent risk factor for cardiovascular disease. It is deemed better than traditional lipidic indicators for prognostic value. Current hypolipemic drugs have little effect in Lp (a) concentration. We have studied the lipoprotein profile in two groups of patients after partial correction of anemia. Fourteen males aged between 50 and 75 years were treated with nandrolone decanoate (200 mg/week for six months) and 12 patients (8 females and 4 males) between 23 and 79 were treated with erythropoietin (EPO; 200 U.I. subcutaneously, posthemodialysis). The increase of hemoglobin was similar in both groups: 10.8 ± 1.7 vs. 7.9 ± 0.9 g/dl in the Androgen group, and 10.8 ± 1 vs. 7.7 ± 0.9 in the EPO group ($P < 0.01$ in both groups). We recorded an Apo B increment (141 ± 51 vs. 121 ± 30 mg/dl) and HDL2 cholesterol reduction (5 ± 3.9 vs. 13.1 ± 11.9 mg/dl) in the Androgen group ($P < 0.05$), and no significant variations in cholesterol, triglycerides, Apo A, and HDL3 cholesterol. However, the most relevant finding was a 74% reduction in Lp (a) levels (7.1 vs. 19.8 mg/dl, median, $P < 0.01$). Lp (a) concentration decreased in all but three patients, who had a very low Lp (a) basal concentration (less than 7 mg/dl). We did not notice any correlation between Lp (a) and other lipidic parameters or hemoglobin variations. Changes in the lipidic profile were reversed two months after nandrolone suspension. In the EPO group, we did not record changes in the lipidic profile after partial correction of anemia. Androgens cause an important decrease in Lp (a) serum concentration in hemodialysis patients. This action is independent on the effect on anemia and could have therapeutical impact in selected groups.

Abnormalities in lipoproteins in hemodialysis patients: Comparison of low molecular weight heparin (LMWH) vs standard heparin (SH). *R. Perez-Garcia, L. Rovina, E. Verde, C. Vozmediano, F. Anaya, E. Junco, M. Ortiz, F. Valderrabano, Service Nefrologia, Hosp. Gregorio Marañon, Madrid, Spain.* The aim of this study was to compare lipid parameters, including Lp(a), between patients on hemodialysis (HD) with LMWH and SH as anticoagulant. Thirty-two patients, 18 men and 14 women, with a mean age of 58 ± 16 (28–80) years (mean ± SD) on HD were studied. The HD schedule was 3 hours, 3 times per week, blood flow 350–400 ml/min, using in 15 of patients high flux dialyzers. All of them were with bicarbonate dialysate, containing glucose 1.5 g/liter. The patients were randomly assigned to one of two groups. In Group LMWH, 16 patients were changed from SH to LMWH as anticoagulant treatment for HD for a year. Group SH, 16 patients continued on SH, as control group. Serum lipid parameters and atherogenic risk ratios were measured at basal, first, 2nd, 3rd, 6th and 12th months, pre- and post-HD. During the basal time 11 out of 32 patients had increased serum triglycerides and 8 hypercholesterolemia. Patients had decreased levels of ApoA1 and HDL cholesterol and increased levels of Lp(a) compared to controls. Hypertriglyceridemia was more frequent in diabetics (7/12). Total dosage of SH per session (54.3 ± 9.4 UI/kg) did not change in group SH during study; in the patients of group LMWH the total dose of LMWH per session was 38.6 ± 13.2 UaXa/kg (70% previous dose) with sufficient anticoagulation obtained at all times. The total cholesterol decreased significantly ($P < 0.01$), to a mean value of 26 mg/dl at 1 year in patients of group LMWH but not in group SH. HDL cholesterol decreased significantly ($P < 0.01$), to a mean value of 5 mg/dl at 1 year in both groups. Serum triglycerides, LDL/HDL, LDL/ApoB, HDL/ApoA1, and total cholesterol/HDL did not change in any group during study follow-up. We observed a raised Lp(a) concentration in HD patients, 42.3 ± 61 mg/dl, compared to controls, with a high variability between each patient. The Lp(a) did not appear to be affected by change from SH to LMWH. No correlation between the Lp(a) level and other lipid parameters was found. In conclusion, a significant decrease in total cholesterol level in the group with LMWH was found, but without changing either atherogenic risk ratios or Lp(a) levels.

Does the activation of the antiproteinase system depend on the biocompatibility of the hemodialysis membrane? *R. Bustamante, A. Mendiluce, J. Nuñez, J.M. Briso-Montiano, N.S. Jabari, J.A. Herruzo, L. Sanchez, J. Bustamante, Servicio de Nefrología, Hospital Universitario, Valladolid, España.* Nine plasma proteins control the proteolytic activity in blood and tissues. The α_1 antitrypsin and the α_2 macroglobulin are the principal plasma anti-proteins that inactivate proteolytic activity, cancelling the granulocyte elastase. Plasma levels were studied in 25 patients (aged 40 ± 5.6 years) who have used various dialyzers for 48 ± 13 months throughout hemodialysis, at 0, 15, 30 120 and 240 minutes of the procedure: 10 patients used cuprophan, 5 polyacrylonitrile (PAN), 5 ethylenvinyl alcohol (EVAL) and 5 patients used polysulfone dialyzers. The determination of the granulocyte elastase was accomplished by enzymoimmunoassay, and that of the α_1 antitrypsin and α_2 macroglobulin by nephelometer. A significant increase ($P < 0.001$) of the granulocyte elastase was produced in the 4 groups in relation to the levels before hemodialysis. The α_1 antitrypsin is lower in all the groups in relation to the predialysis levels, but the decrease was significant only in the cuprophan group ($P < 0.05$). The α_2 macroglobulin was lowered in the four groups in relation to the control levels at the start of the procedure, the decrease being significant only in the cuprophan group ($P < 0.001$). During the hemodialysis the granulocyte elastase was not significantly modified with the polysulfone membrane; however, it was significantly increased ($P < 0.01$) from 30 minutes on in the groups using EVAL, PAN, and cuprophan dialyzers. In conclusion, the decreases in the α_1 antitrypsin and the α_2 macroglobulin are more important in the cuprophan group, where the elevations of the elastase are greatest. The decrease may be due to the antiproteasas effect on the granulocyte elastase. This phenomenon also occurs in the other three groups, but with lesser values.

HCV infection in dialysis. Results of the Spanish four-year prospective study. *HCV Spanish Study Group, G. Barril and J.A. Traver (Co-ordinators) Department of Nephrology, Hospital Universitario de la Princesa, Madrid, Spain.* Since 1991 until 1994, we prospectively studied the prevalence of HCVAb in 91, 88, 88 and 97 Spanish centers, respectively. The number of patients has been 5228, 5441, 5644 and 6581, respectively, meaning a 43% of the global Spanish dialysis population. The study parameters included: type of renal replacement therapy (RRT) (hemodialysis, HD, in hospital, satellite unit, home HD or CAPD), number of seroconversions each year and new HCV(+) patients initiating RRT. The prevalence in the renal unit staff and the risk to develop HCV Ab after professional accidents were also evaluated. Results are shown in the table.

	1991	P	1992	P
Total	33.1%	<0.05	31.1%	<0.001
HD	36%	<0.05	33.7%	<0.001
HD Hospital	36.3%	<0.05	33.8%	<0.001
HD Satellite Unit	35.4%	NS	33.5%	<0.001
Home HD	17.6%	NS	17%	NS
CAPD	10.6%	NS	13.4%	NS

	1993	P	1994
Total	25.8%	NS	25.2%
HD	28%	NS	27%
HD Hospital	28.2%	<0.05	26.4%
HD Satellite Unit	27.5%	NS	28.5%
Home HD	16.6%	<0.05	32.3%
CAPD	11%	NS	20.5%

The incidence has been 2.86, 1.39 and 1.29, respectively. There is a high prevalence of new HCV(+) patients initiating RRT (362 in three years). The number of centers that have adopted isolation measures has increased during these four years (21, 29, 43 and 51, respectively). In spite of these measures, a considerable number of patients seroconvert each year, though during last two years the number of seroconversions has decreased (141 in 1992, 79 in 1993 and 85 in 1994), regardless of a higher dialysis population. In these four years, 149 accidents have been reported and 4 of those cases have become VHC (+). Nurses are the staff most exposed to this risk of infection. We conclude that the prevalence of VHC is still very high. Even when more centers adopt isolation measures, the number of seroconversions is still important. The high prevalence of VHC (+) in dialysis patients is affected by the high prevalence of the infection in patients initiating RRT. Nurses are at higher risk to be infected by professional accidents than the rest of members of the renal unit staff.

Control of secondary hyperparathyroidism in hemodialysis with oral calcium supplements and low-calcium dialysate. *J.L. Teruel, A.M. Tato, T. Tenorio, R. Marcén, F.F. Liaño, T. Cano, J. Ortuño, Department of Nephrology, Hospital Ramón y Cajal, Madrid, Spain.* The possibility of controlling secondary hyperparathyroidism with low-calcium hemodialysis solution and without calcitriol is widely debated. We studied the evolution of PTH levels in low-calcium hemodialyzed patients treated with oral calcium supplements. Thirty patients who did not previously receive vitamin D supplements began hemodialysis therapy with a low-calcium solution (2.5 mEq/liter). All of them were treated exclusively with calcium carbonate. We assumed that the control of hyperparathyroidism was adequate if intact PTH (iPTH) levels were lower than 250 pg/ml. A global and progressive drop of iPTH levels was observed along the first year in hemodialysis [356 ± 179, basal; 236 ± 183, 3 months; 215 ± 158, 6 months; 215 ± 169, 9 months; and 199 ± 196 12 months; $P < 0.01$ (ANOVA)]. PTH levels increased only in four patients during the first year of treatment, and only two required calcitriol. Serum aluminum concentration at the end of the first year was very low: 7.7 ± μg/liter. At the beginning of the study hyperparathyroidism was controlled in 9 patients (30%), and after 12 months of therapy 22 patients (73%) showed adequate PTH concentration. We did not notice differences in sex, age, initial PTH levels, serum phosphorous concentration, or the calcium-phosphorus product between the two groups. However, the mean serum calcium concentration was significantly lower in patients with hyperparathyroidism (8 ± 1 vs. 9.3 ± 0.6 mg/dl, $P < 0.05$). In conclusions, (1) an appropriate control of hyperparathyroidism is possible with calcium carbonate supplements and low-calcium dialysate (2.5 mEq/liter). (2) Serum calcium concentration is the main factor in hyperparathyroidism evolution.

Trabecular bone mass and 2.5 mEq/liter dialysate calcium concentration in hemodialysis patients with nonaluminic adynamic bone disease. *M.C. Sánchez Perales, M.J. García Cortes, S. Fernández Martinez, P. Pérez del Barrio, F. Borrego Utiel, V. Pérez Bañasco. Servicio de Nefrologia, Hospital General de Especialidades, S. Radiologia, Jaén, Spain.* Nonaluminic adynamic bone disease is known to be associated with low PTH secretion. Positive balance calcium (Ca) by calcium carbonate or dialysate calcium concentration (DCa) might play a role in the parathyroid gland suppression, and a decrease in DCa to 2.5 mEq/l or lower has been proposed. Its long-term effect on bone mass has not been established. The aim of the present study was to evaluate the effect of lowering calcium dialysate in bone mass by computed tomography (QCT) in hemodialyzed patients with nonaluminic adynamic bone disease. We prospectively studied 22 patients with intact PTH below 120 pg/ml, using 3 mEq/liter DCa and CaCO3 as the sole phosphate binder. None of them had previous renal transplantation, aluminic toxicity nor had undergone parathyroidectomy. They were randomized in two groups (GI and GII), with similar age, sex, and time on dialysis. There were no differences among groups in the levels of PTH, Ca, P (phosphate) and PA (alkaline phosphatase). Group I ($N = 12$) was transferred to 2.5 mEq/liter DCa and Group II ($N = 10$) continued using 3 mEq/liter. Bone mineral density (BMD) of the lumbar spine was assesed with single energy computed tomography at basceline (no differences among groups) and 12 months later. Ca, P and PA were measured monthly and PTH every three months during one year. Results: Three patients did not conclude the study.

	GI ($N = 11$) DCa 2.5 mEq/liter	GII ($N = 8$) DCa 3 mEq/liter
BMD B/F[a]	133 ± 49/111 ± 46 $P < 0.05$	146 ± 53/146 ± 46
PTH B/F	43.1 ± 23/100.6 ± 68 $P < 0.05$	47.9 ± 30/80.1 ± 54.7
Ca B/F	10.55 ± 0.8/10.0 ± 0.8	10.77 ± 0.9/10.02 ± 0.7
P B/F	5.0 ± 0.99/5.9 ± 0.95	4.54 ± 1.91/5.76 ± 1.68
PA B/F	121 ± 46/152 ± 38.5 $P < 0.05$	123 ± 41/137 ± 40.3
CaCO3/ Accum/ Day	1633 ± 964 g// 4.54 ± 2.6 g/day	1086 ± 987 g // 3.01 ± 2.7g/day

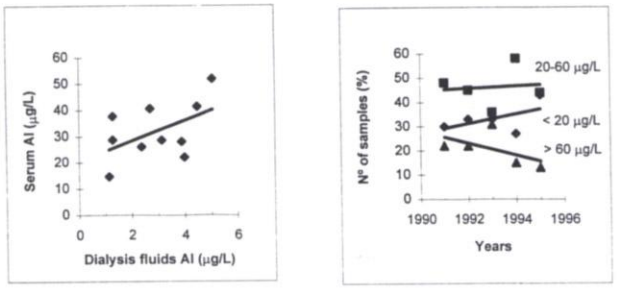
Abbreviations are: B, baseline; F, final.
[a] mg/cc; Ca and P, mg/dl; PA, UI/liter; Intact PTH, pg/ml.

In conclusion, the use of 2.5 mEq/liter dialysate calcium concentration in hemodialysis patients with nonaluminic adynamic bone disease resulted in: (1) loss of trabecular vertebral bone mass measured by QCT; (2) increase in PTH secretion and biochemical markers of bone formation (PA); (3) a greater calcium carbonate dose.

Treatment of secondary hyperparathyroidism with intravenous (i.v.) calcitriol. Factors related with the lack of response to treatment. *M. Goicoechea, M.C. Vozmediano, R. Perez Garcia, MI. Vazquez, MA. Ruiz, E. Verde, F. Valderrabano, Department of Nephrology, Hospital Gregorio Marañon, Madrid, Spain.* Intravenous calcitriol is know to directly suppress PTH secretion and release. However, there is confusion nowadays regarding the therapeutic handling of intravenous calcitriol and about the factors implicated in the lack of response. We studied 36 hemodialysis patients (18 males and 18 females) with moderate-to-severe hyperparathyroidism (iPTH 836 ± 58 pg/ml, mean ± SEM), who underwent treatment with i.v. calcitriol at starting doses of 2 μg after each hemodialysis session. The mean follow-up time was 9.2 ± 2.3 months. Two patients were excluded of the study because they receiving a kidney transplant. All of them were dialyzed with bicarbonate hemodialysis and a calcium concentration of 2.5 mEq/liter in the dialysate. Twenty-five patients (73.5%) responded adequately to the treatment, with PTH levels lowered more than 50% (Group A). Nine patients (26.5%) did not obtain the 50% lowering of PTH (Group B). In group A, 12 out of 25 patients were able to maintain PTH levels to about 250 to 300 pg/ml (Group A1) and 13 of them were not able to do so (Group A2). Total serum calcium increased significantly in the responder patients (from 9.8 ± 0.15 to 11 ± 0.3 mg/dl) as did serum phosphate in the nonresponder patients (from 5.7 ± 0.5 to 11 ± 0.3 mg/dl). Pretreatment serum iPTH (951 ± 91 vs. 650 ± 60 pg/ml) and alkaline phosphatase (632 ± 89 vs. 329 ± 37 IU/liter) were significantly higher in Group A2 patients vs. Group A1. Hypercalcemia appeared in 23 patients (64%) and hyperphosphoremia in 20 patients (55.5%). Hypercalcemia was more frequent between patients from Group A1 (69%) and A2 (66%). Hyperphosphoremia was more frequent between patients from Group A2 (62%) and Group B (78%). Patients who developed hypercalcemia and hyperphosphoremia had a higher pretreatment serum calcium (10 ± 0.12 vs. 9.5 ± 0.2 mg/dl) and serum phosphate (6.3 ± 0.3 vs. 4.9 ± 0.2 mg/dl) than the rest of the patients. In conclusion, i.v. calcitriol

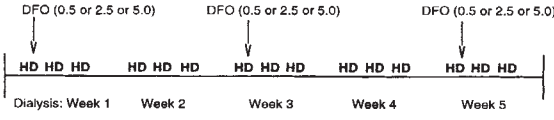
suppresses PTH secretion in patients with severe secondary hyperparathyroidism, but long-term complications due to therapy limits its therapeutic use. The absence of response to i.v. calcitriol is mainly associated with a poor control of serum phosphate levels.

Longitudinal multicenter study (1991–1995) of aluminum concentration in dialysis fluid: Effect on serum aluminum. *C. Díaz-Corte, M.A. Canteros, J.L. Fernández-Martín, M. Serrano, S. Barreto, J.B. Cannata, Bone and Mineral Research Unit, Instituto Reina Sofía de Investigación, Hospital Central de Asturias, Oviedo, Spain.* Aluminum (Al) intoxication had its maximum incidence in the last decade. Although the acquisition of effective measures of prevention have significantly reduced its prevalence, recent studies show that despite of such measures, in most of the European countries and USA about 20% of patients still have high values of serum aluminum and/or are diagnosed of Al overload. The aim of this work was to analyze the evolution of Al in dialysis fluid and in serum throughout last 5 years in 10 Spanish centers (total number of samples = 3458). Throughout the 5 years the mean of aluminum in dialysis fluid was of 3.82 μg/liter (range: 1.0 to 86.1 μg/liter). The percentage of samples with low Al (< 2 μg/liter) was 59.6%, with borderline Al (2–6 μg/liter) 25.4%, and with high Al (> 6 μg/liter) 15.1%. Independently of other likely sources of Al exposure (ex. oral) the changes of Al in the dialysis fluid have influenced the levels of serum Al. Along the 5-year follow-up period only 33.2% of patients maintained serum Al lower than 20 μg/liter (normal values), 46.2% had values between 20 and 60 μg/liter (borderline) and 20.6% had high levels (>60 μg/liter). Through the 5 years of follow-up we noticed a decrease in the highest values of serum Al, but not in the other groups.



These results show that still is necessary to make efforts to reduce even more the concentration of Al in dialysis fluid with the objective that the majority of our patients can reach serum Al levels lower than 20 μg/liter.

Ultrafiltrable aluminium after very small doses of desferrioxamine (DFO). *A. Canteros, C. Díaz-Corte, J.L. Fernández-Martín, E. Gago, C. Merayo and J.B. Cannata, Bone and Mineral Research Unit, Renal Unit, Instituto Reina Sofía, Hospital Central de Asturias, Oviedo, Spain.* The treatment of aluminium (Al) overload is based on strict policies of prevention of Al exposure and on effective removal of the metal by means of increasing the ultrafiltrable (dialysable) Al with DFO. Even though it has been suggested that 5 mg/kg of DFO are effective removing Al, recent *in vitro* published results demonstrate that even lower doses can be useful. The aim of this study was to evaluate and compare the amount of ultrafiltrable (dialyzable) Al achieved in 5 hemodialysis (HD) patients (mean basal serum Al, 44.6 ± 16.6 μg/liter) who sequentially received and once per week, 3 different doses of DFO (5.0, 2.5, and 0.5 mg/kg) throughout the 5 week study, according to the following scheme. The order of the three different doses was randomly assigned (0.5, 2.5 or 5.0 mg/kg).



All doses were effective achieving a significant increase in the percentage of ultrafiltrable aluminium (Table).

	Pre-DFO	Post-DFO (0.5)	Post-DFO (2.5)	Post-DFO (5.0)
Ultrafiltrable Al %	14.6 ± 6.9	45.6 ± 11.7	55.6 ± 8.2	58.4 ± 5.9

The results demonstrate that a dose lower than 5.0 mg/kg/week, even ten times lower at 0.5 mg/kg/week, could be used to efficiently remove Al from Al-intoxicated patients. The use of such a small dose may definitely avoid any adverse effect of DFO, also give more flexibility to use DFO due both to the short time of infusion and also to the possibility of using different schedules of administration.

Erythropoietin's role in the immunity of hemodialyzed patients. *R. Bustamante, M. Arranz, J. Nuñez, A. Mendiluce, N.S. Jabary, J.A. Herruzo, J. Martin, J. Bustamante, Servicio de Nefrología, H. Universitario, Valladolid, Spain.* Human recombinant erythropoietin (rh-Epo) seems to affect the immunity of uremic patients. To partially evaluate this, we studied interleukin 2 soluble receptors (IL2-R), lymphocytes and lymphocyte subpopulations in 20 subjects; 10 hemodialysis patients treated with rh-Epo and 10 hemodialysis patients without this treatment were analyzed and compared. The mean ages were 53 ± 14.7. There were 9 males and 11 females who were dialyzed with non-cellulose membranes with 1 m^2 surface area, 4 hours 3 times per week. The two groups were similar in age, sex, and hemodialysis techniques. Samples drawn at 9 a.m. in all patients. Lymphocytes were determined by standard laboratory methods, lymphocyte subpopulations by immunofluorescent staining with monoclonal antibodies, and IL2-R and EPO levels by ELISA. The mean doses were 45 U/kg after HD. The plasmatic levels of EPO and hematocrit (Hct) were similar for the two groups (with Hct 28.7 ± 3.2% and 28.9 ± 5.4% and hemoglobin 9.6 ± 1.3 mg% and 9.4 ± 1.8 mg%. We did not see a significant decrease of IL2-R in the group with rh-Epo treatment. There was a significant decrease of the T4 lymphocyte and T4 cells/T8 cells ratio ($P < 0.05$) in the group with rh-Epo treatment. In this group EPO levels had a significant correlation with T lymphocyte levels. In conclusion, there was a decrease of T4 cells and the T4/T8 cell ratio, and a nonsignificant decrease of IL2-R.

Lipoprotein (a) levels in maintenance hemodialysis (HD): Modifications with rh-EPO treatment. *M. Arranz, R. Bustamante, N. Jabari, L. Sanchez, A. Mendiluce, J. Nuñez, J. Herruzo, J. Bustamante. Servicio de Nefrología, H. Universitario, Valladolid, Spain.* Alterations in the lipidic profile are shown in hemodialysis. To partially evaluate this we studied 19 HD patients (9 males and 10 females), the mean age of whom was 56.2 years; 9 had rh-Epo treatment, 9 had diabetes mellitus and 10 control HD patients. The hemodialysis techniques were similar but with bicarbonate or acetate (AC)-containing dialysis solutions. Triglycerides and cholesterol were determined by enzymatic methods, HDL and VLDL + LDL by electrophoresis, Apo A, Apo B, ApoE and Lp(a) by nephelometric method, and EPO by ELISA. The Lp(a) levels were lower in the group with EPO treatment (30.7 ± 2 vs. 68.2 ± 5 mg/dl, $P < 0.01$) and were greater in the diabetic group (64.2 ± 43.6 vs. 38.5 ± 31, $P < 0.01$). The HDL level was greater in HD with AC (46.8 ± 2 vs. 27.3 ± 3) and in the diabetic group (36.2 ± 6 vs. 27.7 ± 3, $P < 0.05$). The VLDL + LDL levels were lower in HD with AC (65.9 ± 5.6 vs. 73.6 ± 3, $P < 0.01$), and there was a significant decrease in the group without diabetes (65.1 ± 6 vs. 76.2 ± 1). Apo A was greater in HD with AC (147.6 ± 33 vs. 119.5 ± 22) ($P < 0.005$) and with diabetes (151.1 ± 9 vs. 44.9 ± 1, $P < 0.001$). In conclusion, there was a significant increase of Lp(a) levels in diabetic patients and HD patients receiving rh-EPO treatment. We saw a significant decrease of HDL and VLDL + LDL levels in the group with rh-EPO treatment and diabetes.

Relationship between the intensity of hemodialysis and the response to erythropoietin. *M.J. García Cortés, M.C. Sánchez Perales, F.J. Borrego Utiel, P. Pérez del Barrio, J. Borrego Hinojosa, V. Pérez Bañasco, S. de Nefrología, Hospital Gral de Especialidades, Jaen, Spain.* Several causes of resistance to erythropoietin (EPO) in hemodialysis patients have been defined, but the contribution of uremic inhibitors of erythropoiesis to this resistance is unknown. This study was designed to assess the relationship between the intensity of hemodialysis and the response to erythropoietin therapy in hemodialysis. Seventy-five hemodialysis patients treated with EPO, with

initial serum ferritin >80 ng/ml and MVC 80–100 fl were divided in two groups: GI, KtV < 1.3 (N = 59) and GII, KtV ≥ 1.3 (N = 16). Hemoglobin, Hct, ferritin, TS, albumin, aluminium, dose of EPO (U/kg/week), KtV, PCR and URR were measured. The level of dialysis (dialyzer, Qb, duration of each hemodialysis) was increased in GI patients for 12 weeks. At the end of this period the same parameters were estimated. The target Hct was 30%. We found that patients with a KtV < 1.3 needed more EPO than patients with KtV ≥ 1.3 (82.7 ± 43.9 vs. 56.1 ± 27.1 U/kg/week, $P < 0.01$) to maintain the same Hct. There were no differences in aluminium, ferritin and albumin between these groups. After 12 weeks the efficacy of dialysis didn't increase in 11 patients (GA), and it increased in 48 (GB), 32 of them had a KtV of <1.3 at the end of the study (GBI) and 16 had a KtV ≥1.3 (GBII). Hct only increased in those groups in which the efficacy of dialysis increased (GI, GII) without modification of EPO doses.

	GA N = 11	GBI N = 32	GBII N = 16
KtV i/f	1.16 ± 0.12/1.13 ± 0.12[b]	0.97 ± 0.16/1.11 ± 0.12[a]	1.05 ± 0.17/1.40 ± 0.12[a]
Hct i/f	31.0 ± 2.9/30.1 ± 3.6	29.3 ± 3.3/30.9 ± 3.0[c]	28.0 ± 3.2/31.2 ± 2.5[c]
EPO i/f	88.2 ± 53.0/80.1 ± 49.9	77.2 ± 28.5/79.5 ± 33.3	89.9 ± 61.1/74.1 ± 46.3
Inc. KtV	−2.5 ± 2.0%	16.4 ± 21.0%	38.0 ± 31.0%
Incr. Hct	−2.4 ± 10.9%	6.5 ± 15.3%	12.6 ± 16.1%

[a] $P < 0.001$; [b] $P < 0.01$; [c] $p < 0.05$. Abbreviations are: i, initial; f, final; Inc, increase.

In conclusion, (1) inadequate hemodialysis could be a cause of resistance to erythropoietin therapy in hemodialysis patients; (2) hemodialysis efficacy must be monitored in hemodialysis patients who have a suboptimal response to erythropoietin.

Serum transferrin receptors and iron kinetics with ^{59}Fe as indicators of erythpropoietic activity in HD patients with CRF treated with rHuEPO. *J. Deira, M. Martin, S. Sánchez, B. Martín, J.M. Tabernero, Servicio de Nefrología, Medicina Nuclear and Hematología, Hospital Clínico de Salamanca, Spain.* Serum transferrin receptor (TfR) levels serve as a new tool of great use in the evaluation of erythropoietic activity. The serum levels of this receptor are directly related to the activity of the compound, and measurement of TfR values could offer a feasible way to assess eythropoietic activity instead of, or as a complement to, iron kinetic studies using ^{59}Fe. To evaluate both parameters, the following investigation was designed. In 22 patients on HD we evaluated erythropoiesis before and at 4 months after treatment with rHuEPO by: (1) hemoglobin (Hb) in g/d liter, hematocrit (Hct) in %, and reticulocytes (Ret); (2) TfR levels in mg/liter; and (3) plasma iron clearance ($T_{1/2}$), plasma iron turnover (PIT) in μmol/liter whole blood/day, and transferrin uptake by the Erythron (ETU) in μmol/liter whole blood/day. The existence of ferropenia, secondary hyperparathyroidism and aluminium intoxication was ruled out.

Day	Hb	Hct	Rct × 1000	TfR
0	9 ± 1.4	26.3 ± 4	75.4 ± 29	2.17 ± 0.8
15				2.68 ± 0.8[a]
30	9.8 ± 1.6	28.6 ± 5	100.8 ± 62	2.97 ± 0.8[a]
45				3.24 ± 0.8[a]
60	10.6 ± 1	31.4 ± 5	95 ± 22.8	3.13 ± 0.7[a]
90	11 ± 1.8	32.4 ± 5	97 ± 35	3.10 ± 0.7[a]
120	11.3 ± 1	33.5 ± 4	77.4 ± 20	2.94 ± 0.8[a]

Day	$T_{1/2}$	PIT	ETU
0	135 ± 49	0.38 ± 0.12	30.4 ± 17
15			
30			
45			
60			
90			
120	97 ± 31[a]	0.53 ± 0.3[a]	49.9 ± 3[a]

[a] $P < 0.05$ vs. day 0

In conclusion, (1) with rHuEPO, blood and TfR values increased, and iron kinetics were activated, with $T_{1/2}$ decreasing and PIT and ETU increasing. These observations point to an increase in erythropoietic activity. (2) In the first stages of the study (day 30 of treatment with rHuEPO) there was a positive correlation between Hb and Hct and TfR levels (r = 0.51) and the number of reticulocytes (r = 0.55). However, this did not occur before initiation of treatment with rHuEPO or in later stages of the study. (3) Although ^{59}Fe kinetics and TfR are useful for assessing erythropoietic activity, the results obtained from their measurement are not equivalent since there was no correlation between TfR levels and iron kinetics either before or after treatment with rHuEPO.

Effect of route of administration of rHUEPO on erythropoietic activity evaluated with serum transferrin receptors (RfT) and iron kinetics with ^{59}Fe in patients on HD. *J. Deira, M. Martin, S. Sánchez, B. Martín, J.L. Lerma, J.M. Tabernero, Servicio de Nefrología, Medicina Nuclear and Hematología, Hospital Clínico de Salamanca, Spain.* Recent reports have highlighted the greater efficacy and lower costs of subcutaneous EPO administration as opposed to the i.v. route. However, the effect of the route of administration on erythropoietic activity remains unknown. The aim of the present work was to evaluate erythropoiesis when EPO was administered s.c. as compared with i.v., studying its activity by analyzing TfR levels and iron kinetics with ^{59}Fe. Eleven patients with "suitable dialysis" parameters on HD were studied. The presence of ferropenia, secondary hyperparathyroidism and aluminium intoxication was ruled out. The patients were treated over four months with EPO s.c. Following this, after informed consent had been granted and a 1 month washout period without EPO had elapsed, the drug was administered again for four additional months, this time with i.v. administration. In all of the patients, the following parameters were measured monthly: (1) usual blood parameters; (2) iron metabolism; (3) basal Tfr levels and these levels at 15, 30, 45, 60, 90 and 120 days in mg/liter, and (4) iron kinetics [plasma iron clearance ($T_{1/2}$), plasma iron turnover (PIT) and transferrin uptake by the Erythron (ETU), both in μmol/L whole blood/day]. The mean dose of s.c. EPO was 24 IU/kg/session; in the i.v. route, this was 31 IU/kg/session.

	Day	0	15	30
Hb	s.c.	9.1 ± 1		10.3 ± 2
	i.v.	9.2 ± 1.2		9.6 ± 1
TfR	s.c.	2.6 ± .9	3.2 ± .7	3.3 ± .6
	i.v.	1.4 ± .4	1.7 ± 3	2.0 ± .4
$T_{1/2}$	s.c.	130 ± 40		
	i.v.	131 ± 49		
PIT	s.c.	.39 ± .12		
	i.v.	0.71 ± .2		
ETU	s.c.	32.4 ± 19		
	i.v.	59 ± 3		

	Day	45	60	90	120
Hb	s.c.		11.1 ± 2*	11.3 ± 1*	11.7 ± 1*
	i.v.		10.6 ± 1*	10.7 ± 1*	10.9 ± .9*
TfR	s.c.	3.4 ± .9	3.4 ± .8	3.3 ± .7	3.3 ± .9
	i.v.	2.1 ± .3	2.0 ± .3	2.1 ± .4	2.0 ± .3
$T_{1/2}$	s.c.				102 ± 25
	i.v.				88 ± 32
PIT	s.c.				0.43 ± .1
	i.v.				0.85 ± .35
ETU	s.c.				37.7 ± 15.8
	i.v.				49 ± 44

* $P < 0.05$ vs. day 0.

Summary and conclusions: (1) Both administration routes elicit a similar increase in Hb; (2) erythropoietic activity was greater and appeared earlier on with the i.v. route as evaluated by RfT values; (3) the iron kinetics parameters point to a similar rise in erythropoietic activity with both routes of administration but do not show in which it was higher; (4) in both groups, an inverse correlation was seen between RfT values and iron deposition. The present findings suggest that the i.v. route elicits greater erythropoietic activity, although Hb levels similar to those obtained with the s.c. route are achieved; this could be interpreted as indication of a component of inefficient erythropoiesis.

Hematocrit level (Hct) and quality of life (QL) in hemodialized patients with rHuEPO. *J.M. Logroño, M.V. Ejea, R. Virto, C. Laviades, Section of Nephrology, "San Jorge" Hospital, Huesca, and Department of Pharmacology, University of Zaragoza, Spain.* The optimum Hct level with rHuEPO remains a matter of debate. Several authors indicated that 30% Hct average can be insufficient and, probably, with Hct levels near to normal can further improve the QL indicators in hemodialized patients (HDP). This was a prospective study designed to assess the QL on two different Hct levels (32 vs. 38%). Nineteen patients (pts; 13M/6F; aged 58 ± 14 years; 5.1 ± 2.5 Friedmand comorbility index) clinically stabilized on HD since 40 ± 31 months treated with intravenous (8p: 3 times/week) or subcutaneous (11p: 2 times/week) rHuEPO, and stable Hct concentration (30–33%) were selected. Afterwards, these pts continued receiving doses of rHuEPO (6.25–12.5 U/kg/day every 4–8 weeks) higher than previously administered until they increased their Hct level to about 38%. The pts acted as their own controls and the study period was for one year. QL was evaluated at the beginning of the study and after 1 year of follow-up using the Karnofsky Scale (KS) and the Sickness Impact Profile (SIP) questionnaire. A high KS score and a low SIP score indicated better QL. Moreover, the iron parameters, the changes blood pressure, the left ventricular mass index (LVMI by Eco Doppler), the efficacy of dialysis (Kt/V) and the thrombosis of arteriovenous fistulae were also regularly analyzed. Data were compared by Wilcoxon and simple regression tests.

Parameters	Prestudy	1 year	*P*
Hematocrit %	32.3 ± 2.9	38.0 ± 2.1	< 0.01
Dose EPO *U/kg/week*	102.3 ± 74.7	135.5 ± 79.9	< 0.01
Route i.v.	135.9 ± 89.5	182.8 ± 96.5	NS (< 0.1)
Route s.c.	68.7 ± 37.2	101.1 ± 43.3	< 0.05
LVMI (8 pts route i.v.)	162.0 ± 52.0	120.9 ± 36.7	< 0.01
Quality of life: SIP			
D. overall	17.0 ± 11.8	14.0 ± 10.9	< 0.01
D. physical	11.9 ± 13.3	8.8 ± 12	< 0.01
D. psychosocial	15.2 ± 12.7	14.0 ± 12.7	NS
Quality of life: KS	68.4 ± 13	73.6 ± 16.4	< 0.05

The categories of SIP that improve significantly were: sleep and rest, mobility, communication and eating.

It is concluded that higher Hct levels during rHuEPO treatment decrease the miocardic mass and improve the QL significantly for most QL indicators used. Moreover, we do not find any clinically important side effects, although the dose of rHuEPO needed to be increased by up to 40% by route i.v. and 50% by route s.c.

Relationship between secondary hyperparathyroidism (HPT) and supraventricular arrhythmias (SVA) in hemodialysis (HD). *E. Verde, A. Pérez de Prado, M.C. Vozmediano, R. Pérez, R. Jofré, J.M. López, E. Junco, M. Barambio, J. Almendral, F. Valderrábano, Department of Nephrology and Cardiology, Hospital General "Gregorio Marañón," Madrid, Spain.* It has been suggested that HPT may play a role in the development of cardiac diseases. Arrhythmias are increased in HD patients (pts) with HPT. Sixty-four pts in sinus rhythm (34 M/30 F; mean age, 58 ± 14 years) were studied with ECG-Holter monitoring during 6 consecutive sessions of HD. The aim of the present study was to analyze the incidence and type of SVA and premature atrial contractions (PAC) in HD. Standard blood tests were taken along HD sessions. Echocardiograms were performed on a non-dialysis day. HD pts were divided into 2 groups according to i-PTH levels; 23 pts had i-PTH levels less than 200 pg/ml (Group A) and the remaining 41 pts had i-PTH > 200 pg/ml (Group B). There were no statistical differences in age, gender and BMI between groups. No differences were found in mean time on dialysis treatment (61 ± 75 vs. 47 ± 53 months; NS). The prevalence of cardiovascular risk factors was similar in the two groups: hypertension (70% vs. 49%); diabetes mellitus (35% vs. 27%) and smoking (56% vs. 49%). No differences were found in left ventricular mass index between groups (177.7 ± 50.4 g/m^2 vs. 191.2 ± 65.1 g/m^2). ECG-Holter results and electrolytic changes are shown in the following table:

	Group A	Group B	*P*
SVA	30%	56%	< 0.05
Significative PAC	26%	65%	< 0.01
K^+ decreased *mEq/liter*	2.35 ± 0.49	2.26 ± 0.73	NS
HCO_3^- increased *mEq/liter*	5.05 ± 1.90	5.39 ± 1.82	NS
Initial Ca^{++} *mmol/liter*	1.05 ± 0.10	1.05 ± 0.08	NS
Final Ca^{++} *mmol/liter*	1.21 ± 0.08	1.14 ± 0.07	< 0.01

In conclusion, HD pts with higher i-PTH levels are prone to develop SVA and PAC. A less pronounced increase of ionic calcium levels along HD may play a significant role in the development of these arrhythmias.

Treatment of anemia with androgens in male patients aged over 50 years. *J.L. Teruel, A. Tato, T. Tenorio, G. Fernández, R. Marcén, F. Liaño, M. Rivera, J. Ortuño, Department of Nephrology, Hospital Ramón y Cajal, Madrid, Spain.* In a retrospective study in hemodialyzed patients treated with nandrolone decanoate, we observed that the anemia response is related to the age of the patients, and excellent results might be obtained in elderly patients. After our observations, in 1990 we instituted the following protocol for the treatment of anemia in hemodialyzed patients: androgens are to be used in male patients aged over 50 years, and recombinant human erythropoietin is to be used in male patients below this age and in women. The aim of this study was to prospectively analyze the effectiveness of androgen therapy in this population. Thirty-nine hemodialyzed patients aged between 50 and 84 years received a cycle of 200 mg i.m. of nandrolone decanoate once a week for six months. The goal was to reach a hemoglobin concentration higher than 9.5 g/liter. We observed a global increase of hemoglobin from 7.4 ± 0.9 to 10.5 ± 2 g/liter ($P < 0.001$). Only two patients did not show an adequate response to androgens, nor to erythropoietin. The target hemoglobin was reached in 28 (72%) patients. In addition to erythropoietic action, we recorded beneficial anabolic effects, such as an increase in dry weight (64.7 ± 10 vs. 66.8 ± 10 kg, $P < 0.001$) and in serum albumin concentration (3.9 ± 0.4 vs. 4.3 ± 0.4 g/liter, $P < 0.01$). Improvement in anemia with androgens did not produce an elevation in blood pressure: blood pressure control improved in three patients and only increased in one patient. We did not see any case of hepatotoxicity associated to the use of nandrolone decanoate. Nandrolone decanoate is a good alternative in the treatment of anemia in elderly male patients on chronic hemodialysis. The anabolic effects may have a therapeutic use in the treatment of malnutrition of dialyzed patients.

Parenteral iron: Distribution in hemodialysis patients. *M.J. García Cortés, F.J. Borrego Utiel, M.C. Sánchez Perales, A. Liebana, P. Serrano Angeles, S. García Marcos, V. Pérez Bañasco, S. de Nefrología, Hospital Gral de Especialidades, Jaen, Spain.* Iron deficiency is the most important cause of resistance to erythropoietin in hemodialysis patients. In order to avoid it we need to know iron stores, iron required to achieve target hemoglobin and efficacy of iron administered. This study attempted to assess the distribution of sodium-ferric gluconate (Na-Fe-G) given intravenously (i.v.). Forty-nine hemodialysis patients with an initial serum ferritin < 200 ng/ml or TS < 20% were treated with Na-Fe-G during the period of two months. Patients with ferritin < 50 ng/ml received 1500 mg divided in 24 i.v. doses; patients with ferritin > 50 or ferritin > 200 and TS < 20% received 500 mg divided in 8 doses. Hemoglobin, ferritin, TS, and iron stores were measured at baseline and revised two months later. Iron stores were estimated by the empirical formula of Cook modified by Anastassiades: Iron stores = 400 * (Ln ferritin i − Ln 50). Iron needed for new hemoglobin synthesis was calculated considering that a rise of 1 g/dl in circulating hemoglobin uses 150 mg of iron. All estimated parameters

increased significantly at the end of the study. A total amount of 915.8 ± 457.4 mg of iron was administered; 119.6 ± 238.7 mg (14.5 ± 33.0%) were used for hemoglobin synthesis and 574.6 ± 507.4 mg (57.1 ± 47.0%) increased iron stores; 221.5 ± 423.1 mg (28.6%) couldn't be measured. It could be due to dialyzer and gastrointestinal losses characteristic in hemodialysis patients. More than 70% of iron administered as Na-Fe-G become measurable as iron stores or used for hemoglobin synthesis.

Androgens in the treatment of anemia in elderly patients on hemodialysis: Effects on lymphocyte subsets. *A. Gascón, A. Orfao, J.J. Belvis, A. López, J. Ciudad, J. Font, E. Iglesias, F. Berisa, S. Nephrology, General Hospital, Teruel, S. Cytometry, University Salamanca, Spain.* Androgens have been used in the treatment of anemia in patients on hemodialysis (HD) for years. Nevertheless, since the introduction of therapy with recombinant human erythropoietin (EPO) its use has practically been abandoned in daily practice. The aim of the present study was to analyze within a group of HD patients, all over 60 years, the influence that androgens have in lymphocyte activation of peripheral blood (PB) CD4 and CD8 T-lymphocytes, as well as in CD19+CD5+ B-lymphocytes, that are inhibiting B-cells of the immunoglobulin formation. We studied 7 patients on HD, with a mean age of 69 years. All patients were in a stable clinical situation and with adequate dialysis criteria. Erythropoietin was suspended 15 days before beginning therapy with nandrolone decanoate. The dose used was 200 mg/week by intramuscular administration. Urologic control previous to treatment was performed; this was done every two months and consisted in digital rectal examination and levels of specific prostatic antigen. Before beginning the first weekly session of HD, and after four months of treatment, we studied the PB lymphoid subsets. PB samples were analyzed by three-color flow cytometric analysis. The distribution of the subsets analyzed are shown in the followings tables (absolute numbers of cells/μl, and percentage in brackets):

	CD4+	CD4+ CD25+	CD4+Ia+	CD4+ CD25+Ia+
Basal	717 (41%)	448 (64%)	99 (13%)	36 (5.7%)
Mes 4°	608 (36%)	184 (32%)	72 (14%)	20 (3%)
P		<0.005		<0.05

	CD8+	CD8+ CD25+	CD8+Ia+
Basal	398 (22%)	25 (6%)	111 (25%)
Mes 4°	381 (21%)	8 (2.7%)	121 (32%)
P		<0.05	

	CD8+ CD25+Ia+	CD19+	CD19+ CD5+
Basal	1 (0.3%)	91 (5.6%)	37 (42%)
Mes 4°	2 (0.8%)	72 (4.8%)	14 (20%)
P		<0.05	<0.002

This table reflects a significant decrease in the activated CD4 T-cells (CD4+/CD25+ and CD4+/CD25+/Ia+), which would be in relation to a lower level of lymphoid preactivation. There is also a significant decrease in CD8+/CD25+ T-cells. Furthermore, we observed a significant decrease in the CD19+/CD5+ B-cells, which seem to play a part in inhibiting the production of immunoglobulins. HD induces a Th1-type of immune response (increased secretion of IL-2 and INF-γ) that is characterized by increasing cytotoxicity and inhibiting immunoglobulin production. Th1 seems to become inhibited by androgen therapy for this type of immune response. In conclusion, androgen therapy of anemia in HD as well as increasing erythropoiesis seems to provide an immunologic benefit by lowering levels of lymphocyte preactivation of CD4+ and CD8+ T-lymphocytes. It also lowers CD19+/CD5+ B-lymphocytes, which can inhibit imunoglobulin formation.

Androgens in the treatment of anemia in aged patients on hemodialysis: effects on nutritional parameters. *A. Gascón, J.J. Belvis, J. Font, A. Pérez, V. Rubio, F. Berisa, Service of Nephrology, Obispo Polanco General Hospital, Teruel, Spain.* Androgens have been used in the treatment of anemia in patients on hemodialysis (HD) for years. Nevertheless, since the introduction of therapy with recombinant human erythropoietin (EPO) their use has practically been abandoned in everyday practice. The aim of the present study was to analyze within a group of HD patients, all over 60 years, the influence that androgens have on nutritional parameters. We studied 7 HD patients, average age 69 years. All patients were in a stable clinical situation and with adequate dialysis criteria. EPO was suspended 15 days before beginning therapy with nandrolone decanoate. The dose used was 200mg/week by intramuscular administration. Patients underwent urologic control previous to therapy; this was done every two months and consisted in performing digital rectal examination and obtaining levels of specific prostatic antigen. Every two months we studied levels of Hgb, Hcto, EPO, ferritin, creatinine, total proteins, albumin, transferrin, cholesterol, HDL and LDL, triglycerides, and apolipoproteins A1 and B. Anthropometric parameters included cutaneous tricipital (CTF) and subscapular fold (CSF), arm circumference (AC) and arm muscular circumference (AMC), weigh (W) and body mass index (BMI).

	Hgb	Hct	EPO	Creat
Pre-Tto	10 ± 1	30.1 ± 5	10.9 ± 2	9.6 ± 2
Mes 2°	10.7 ± 1	31.6 ± 5	14.9 ± 3	12.7 ± 2
Mes 4°	11.3 ± 1	33.4 ± 6	20.3 ± 13	12.7 ± 3
			$P < 0.02$	$P < 0.005$

	Pro Tot	Album	Transferri
Pre-Tto	6.6 ± 1	3.9 ± 0.4	173 ± 15
Mes 2°	6.7 ± 1	3.7 ± 0.3	175 ± 40
Mes 4°	6.7 ± 1	4 ± 0.1	216 ± 36

	Cholest	HDL	LDL
Pre-Tto	216 ± 52	43 ± 12	136 ± 51
Mes 2°	216 ± 63	29 ± 4	138 ± 47
Mes 4°	214 ± 58	28 ± 7	135 ± 54
		$P < 0.005$	

	Triglic	AP-A1	AP-B
Pre-Tto	169 ± 102	206 ± 23	112 ± 43
Mes 2°	214 ± 120	120 ± 14	114 ± 35
Mes 4°	288 ± 199	100 ± 24	104 ± 40
		$P < 0.0001$	

	CTF	CSF	AC
Pre-Tto	11.2 ± 2	15.6 ± 6	28.9 ± 2
Mes 2°	12.1 ± 3	15.8 ± 6	30.2 ± 2
Mes 4°	10.4 ± 3	16.4 ± 7	30.5 ± 1
			$^*P < 0.01$

	AMC	Weight	BMI
Pre-Tto	25.3 ± 1	69.1 ± 9	25.9 ± 2
Mes 2°	26.4 ± 1	70.6 ± 9	26.6 ± 2
Mes 4°	27.2 ± 1	70.7 ± 9	26.9 ± 2
	$^*P < 0.05$	$^*P < 0.001$	$^*P < 0.001$

These results show that androgens increase levels of Hgb and Hct even in patients like ours who have extremely good levels from the beginning. Endogenous EPO increases in a significant way. We observed an increase in the muscular mass of these patients, with significant increases of creatinine, AC and AMC. Levels of total proteins remained stable or even increased, as was true with albumin and transferrin. As for lipid metabolism, the results were less positive; there was an increase in triglyceride

levels and a significant decrease in HDL and apo-A1 levels. Androgens may be an alternative to EPO in elderly male patients on HD, because the nutritional parameters of these patients are improved with this treatment. However, one must keep a close watch upon the prostatic and lipid parameters.

Hemodynamic response of radiocephalic fistula to different diameter dialysis needles. *E. Gallego Valcarce, J.M. Portoles, F. Llamas, A. Serrano, S. Tallon, E. Andres, C. Gomez, E. Olivas, L. Sanchez Tarraga; Servicio de Nefrologia, Hospital General Albacete, Spain.* We studied the influence of different needles (14 and 15 gauge (G)) producing different blood flow rates (BRFr) on diverse parameters: venous pressure (VP), arterial blood pressure fall (AP), actual blood flow rate (BFRa), recirculation and dialysis efficacy. Eighteen patients were studied: 16 men and 2 women. Mean age was 54.3 ± 17.38 years. Mean time on dialysis was 87 ± 66.5 months.

Hemodynamic parameters	BFRr (ml/min)	200	250	300	350	400
VP (mm Hg)	15G	62.2	81.5	103.5	126.9	149.2
	14G	44.3	59.0	76.0	89.0	109.8
	Reduction PV (%)	28.7	27.6	26.5	29.8	26.4
APfall (mm Hg)	15G	−50	−69	−97	−130	−162
	14G	−31	−44	−64	−85	−108
	Reduction AP (%)	39	37	35	35	34
BFRa (ml/min)	15G	194	239	280	321	359
	14G	194.5	243	288	330	370
	300	350	400			

Recirculations
Method 1: "stop flow". Method 2: Contralateral arm puncture.

	15 G	Method 1	
BFRr (ml/min)	200	300	400
recirculation (%)	0.90	1.20	2.75

	15 G	Method 2	14 G	Method 1
BFRr (ml/min)	200	400	200	300
recirculation (%)	5.07	12.8	1.10	1.32

		14 G	Method 2
BFRr (ml/min)	400	200	400
recirculation (%)	2.54	5.26	12.94

Efficacy was estimated by KT/V = LN (bun pre hd/bun post hd) at BFRr = 400 ml/min, with 15G KT/V = 1.21 and with 14G KT/V = 1.22. No statistically significant differences were appreciated.

Using a 14 G needle instead of a 15 G needle resulted in a reduction of VP from 29.8 to 26.4% for the BRFr range studied. There was also a reduction in AP, which correlated inversely with blood flow. The difference in BRFr and BRFa was always smaller with 14 G needles than 15 G ones. Reduction of blood flow rate with BRFr = 400 ml/min was 7.5% and 10.2% for 14 G and 15 G needles, respectively. There was no statistically significant difference between the recirculation rates obtained with different needles and the same method. The recirculation rates with the same needle and a different method were statistically different ($p < 0.001$) at different blood flow rates (200 and 400 ml/min). Cardiopulmonary recirculation increased when blood flow increased, but fistula recirculation was independent of needle diameter when BRFa were similar. Dialysis efficacy is independent of the needle used if effective blood flow rates and similar recirculation rates are maintained.

Percutaneous hydrodynamic thrombectomy as treatment of acute thrombosis of vascular access for haemodialysys. *J.L. Górriz, J. Palmero, J. Martinez-Rodrigo, L. Pallardó, A. Sancho, E. Alcoy, J. Ramos G.[a] Departments of Nephrology and Radiology. Hospital Dr. Peset. Valencia. Spain.* Traditionally, the treatment of thrombosed access for hemodialysis (HD) has included surgical thrombectomy and operative revision. These procedures lead alter the vascular wall, compromising the feasibility of new vascular access. Other therapies, such as fibrinolitic thrombolysis, are not free of undesirable complications. The aim of our study was to evaluate the results of a new technique, percutaneous hydrodynamic thrombectomy (PHT), for the treatment of recent vascular access thrombosis. PHT was performed by introducing a double-lumen catheter with a distally located large side-hole and rounded tip through the thrombosed access. Saline solution was injected at a constant flow rate, and when the Venturi effect created a turbulence, the clot was removed by suction. Underlying stenoses were evaluated after angiography, and angioplasty was done when indicated. We used PHT in 20 consecutive chronic HD patients admitted to our hospital because of acute vascular access thrombosis (13 Brescia-Cimino arteriovenous fistulae (BC) and 7 PTFE grafts). Mean age was 58 years (range 40–80), months in HD 51 (range 2–154). Eleven patients recived erythropoietin (hematocrit: 30.3 ± 0.7%, range 26.4–32.2%). Three patients were excluded from the study because of the presence of phlebitis or aneurysmatic fistulae. PHT removed the clots in 17 patients (100%) all of whom had more than 60% stenosis of the lumen. Three patients had stenosis greater than 6 cm, and were referred to a surgeon. In the 14 remaining patients, percutaneous angioplasty was performed; a stent prosthesis was placed in 2 patients. Seven patients had early occlusion (< 48 hours), with successful results in the remaining 7 (4 BC, 3 PTFE). Cumulative primary patency was 41%. Mean duration of patency has been 150 ± 86 days (range 47–276). One of the patients had an occlusion 71 days after PHT. In the first HD performed after PHT, blood flow was 287 ± 30 (range 240–350) ml/min with a venous pressure of 147 ± 27 (range 110–180) mmHg. There were no relevant undesirable side effects related to the technique. In conclusion, PHT has been shown an effective treatment for recent thrombosis of HD vascular access, with no associated side effects.

Recirculation of central venous double lumen catheters for hemodialysis. *M.R. Palomar, C. García-Cantón, A. Moreno, A. Toledo, S. Suria, P. Rossique, N. Esparza, T. Hernández, F. Martínez, M.D. Checa. Departments of Nephrology and Radiology, Hospital Insular de Gran Canaria, Las Palmas, Spain.* To determine whether the site of insertion of double lumen catheters for hemodialysis has any influence on recirculation, we performed 50 recirculation tests on 43 catheters in 35 patients. Nineteen of them had chronic renal failure and had no vascular access available and the other 16 had acute renal failure. The types of catheters used and the sites of insertion were as follows: 10 double lumen Hickman catheters (13.5 French and 36 cm long) in the internal jugular vein, 6 double lumen Mahurkar catheters (11.5 French and 19.5 cm long) in the subclavian vein, 7 double lumen Mahurkar catheters (11.5 French and 13.5 cm long), 4 in the subclavian vein and 3 in the internal jugular, 16 double lumen Mahurkar catheters (19 cm long) in the femoral vein and 3 double lumen Hickman catheters in the femoral vein. We performed the urea recirculation test 20 minutes after the beginning of the dialysis session with the pump at 200 ml/min by taking arterial, venous and peripheral blood samples simultaneously and using the formula (Up–Ua/Up–Uv)*100. To analyze the results we considered catheters inserted in subclavia or the jugular vein separately from those inserted in the femoral vein. The mean rate of recirculation was 9.2 ± 12%, $N = 50$; it was significatively higher in the femoral vein (14.5 ± 15% $N = 24$) than in the subclavian or jugular (5.2 ± 6%, $N = 26$, $p < 0.01$). There was no significant difference between the subclavian (3.1 ± 3%, $N = 10$) and jugular (6.6 ± 7%, $N = 16$). No difference was observed between the type of catheter used in subclavian and jugular veins: Hickman 6.9 ± 7%, $N = 12$, Mahurkar of 13 cm, 3.6 ± 5%, $N = 8$, Mahurkar of 19 cm, 4.1 ± 4% $N = 6$. In a 14-patient subgroup with catheters inserted at the femoral site we repeated the recirculation test with patients' inferior limbs at 45°, there was a significant reduction in recirculation rate, 19 ± 17% vs 7 ± 6%, $P < 0.01$. We conclude that catheters in femoral veins have a higher recirculation rate than the ones located in subclavian or internal jugular veins. This should be taken into account when prescribing the dialysis dose, as it could be less effective with femoral access. The higher recirculation rate of the femoral catheters seems to be related to postural changes that improve inferior cava vein

blood flow, as can be appreciated when inferior limbs are at 45° and blood flow is impaired.

Comparative study of hemodialysis catheter infection with and without subcutaneous tunnel. *M. Ramirez de Arellano, F. Bella, MA. Morera, M. Chine, M. Fulquet, R. Cano, X. Cuevas, Nephrology, Internal Medicine and Microbiology Departments, Hospital de Terrassa, Barcelona, Spain.* To explore the incidence of hemodialysis catheter infection and to compare tunnel catheters (TCs) with non–tunnel catheters (NOTCs), we conducted a prospective study for a period of 41 months (May 1992–October 1995). Ninety catheters were inserted in 54 patients; 18 of these catheters were subcutaneous tunnel silastic twin catheters inserted according to "Canaud's" technique (Jugular vein = 10, femoral vein = 8) and 72 were NOTCs, double lumen polyurethane (Jugular vein = 15, femoral vein = 14 and subclavian vein = 43). All catheters were studied in intravascular segment culture with the semiquantitative method described by Maki. We carried out cultures of the skin swabs and the catheter connections as well as blood cultures when there was suspicion of infection. A catheter was considered infected when Maki's culture evidenced ≥15 colony forming units and bacteremia was considered present when the same microorganism was isolated from the blood culture and in the intravascular segment, in the absence of another primary infection focus. Fourteen of 90 catheters (15.5%) were infected, and 5 of these demonstrated bacteremia (35.7%). The isolated microorganisms were: *S. epidermidis* (64.2%), *S. aureus* (35.7%) and *E. faecalis* (7.1%). Infected TCs had an average duration of 71.6 ± 54.2 days and infected NOTCs 32.1 ± 17.3 days.

Infection Incidence

	TC(10) = 1262 days	NOTC(72) = 1834 days
Infection	6 (4.72[a])	8 (4.36[a])
Bacteremia	2 (1.57[a])	3 (1.63[a])

Infection Incidence by Location

	TC (18)		NOTC (29)	
	jugular (10)	femoral (8)	jugular (15)	femoral (14)
Infection	4 (5[a])	2 (3[a])	5 (6.9[a])	1 (16.1[a])
Bacteremia	2 (2.5[a])	0 (0[a])	1 (1.3[a])	1 (16.1[a])

[a] = episodes per 1000 catheter days

In conclusion, Canaud's type subcutaneous tunnel hemodialysis catheter does not appear to reduce the infection incidence seen with temporary NOTCs.

Catheterization of the femoral vein for ambulatory hemodialysis. *X. Cuevas, M. Ramírez de Arellano, M. Fulquet, M. Chiné, R. Cano, R. Samo, and J. Viladoms, Department of Nephrology, Hospital de Mollet, Hospital de Terrassa, Barcelona, Spain.* The catheterization of the femoral vein to provide temporary vascular access for hemodialysis (HD) is a widely known technique, but the anatomy of the area and the use of semirigid catheters make this method applicable only to bedridden patients or to those who need a limited number of HD sessions with the same catheter. Using a subcutaneous tunnel silicone catheter (TSC), we explored the viability of the femoral vein as a vascular access route in ambulatory patients. In 9 patients (4 men and 5 women, mean age 73 ± 11 years), we placed 14 TSCs (7 for end-stage renal disease and 2 for acute renal failure), implanting two double catheters on 3 occasions and one catheter on 8 occasions. We placed the catheters according to Canaud's technique: percutaneous puncture of the femoral vein (7 left side and 7 right side) and subcutaneous tunneling of the catheter (15 cm), with the distal portion showing at the level of the leg, where it is attached to the skin, and the tip of the catheter located in the inferior vena cava. All patients completed ambulatory HD with no limit imposed on movement in or out of bed. With the 14 TSCs, 345 sessions of HD were completed. The blood flow was 200–250 ml/min and the mean venous pressure 166 ± 54 mm Hg. The TSCs were in place for a mean of 67 ± 63 days (range 10–234 days). Eight TSCs (including 2 double catheters) were removed after a mean of 67.8 ± 45 days because internal vascular access was initiated. Four TSCs (including one double catheter) were removed after a mean of 68 ± 110 days because of mechanical obstruction (and coincidental sepsis with *S. Aureus* in one case). One TSC was removed after 86 days by the patient. One TSC was still functioning at the end of the study period, 45 days after placement. Bacteriologic evaluation performed on 10 catheters (71%) showed the previously mentioned double catheter infected with *S. Aureus* and another catheter infected with *S. Epidermidis*. Complications of femoral vein catheterization included two local hematomas (one in association with a double catheter) necessitating blood transfusion and four instances of mechanical obstruction (one involving a double catheter) that had to be removed. Three patients, one of whom had a double catheter, underwent venography after removal of the catheter; no thrombosis of the femoral vein was observed in the iliac artery or inferior vena cava. In conclusion, the cannulation of the femoral vein with a subcutaneous tunnel silicone catheter provided safe vascular access for HD in ambulatory patients without causing functional limitations.

Anticardiolipin antibodies (aCL) in hemodialysis: β2-glycoprotein I dependence and clinical relevance. *C. Bernis, N. Gomez, E. Muñoz de Bustillo, E. Gruss, A. Fernandez, A. Cirugeda, G. Barril, P. Sanz, JA. Sanchez-Tomero, V. Alvarez, and JA. Traver. Nephrology and Hematology Departments, Hospital de la Princesa, U.A.M., Madrid, Spain.* Anticardiolipin antibodies (aCL) purified from patients with autoimmune disease and thrombotic complications have recently been shown to interact with a phospholipid plasma protein, β2-glycoprotein I (β2-GP-I); however, aCL from patients with infections do not interact with β2-GP-I and are not associated with thrombosis. The aim of this study was to determine the incidence of aCL in hemodialysis patients and whether aCL purified from these patients interact with β2-GP-I. We studied 85 hemodialysis patients, 54 males and 31 females. The mean age of the patients was 59 ± 14 years and the mean time on dialysis was 28 ± 39 months. Initial nephropathy, type of dialysis membrane and clinical complications during one year were documented. Blood samples were analyzed for platelet count, APTT, and IgG-aCL and IgM-aCL via ELISA. We performed standard ELISA for aCL (with β2-GP-I) in all patients. We performed modified ELISA (without β2-GP-I) in patients who were positive for aCL on standard ELISA. Positive results on modified ELISA was an indication that aCL were present independent of β2-GP-I. Two patients were positive for IgG-aCL independent of β2-GP-I. In 28 patients (32.9%), the presence of aCL was dependent on the presence of β2-GP-I; 18 of these patients were positive for IgG-aCL (mean value 64 ± 7.8 vs. a normal value of 14 ± 6.5), 10 patients were positive for IgM-aCL (mean value 35.5 ± 8.4 vs. a normal value of 8.4 ± 3.2), and 2 patients were positive for both IgG-aCL and IgM-aCL. There was no correlation between aCL and age, sex, initial nephropathy, length of time on dialysis, or type of dialysis membrane. We observed vascular access thrombosis in 3 of the 28 patients (10.7%) in whom the presence of IgG-aCL and/or IgM-aCL was dependent on β2-GP-I and in 9 of the 57 patients (15.7%) who did not demonstrate aCL (P = n.s.). In conclusion, 32.9% of our hemodialysis patients demonstrated aCL dependent on the presence of β2-GP-I, but they did not show an increased incidence of vascular access thrombosis.

Study of the effect of induction of immunosuppression with OKT3 as compared to conventional therapy using cyclosporine plus corticosteroids in kidney transplantation. *B. Martín, P. García, J.L. Lerma, A. Bondía, L. Corbacho, J.M. Tabernero, Servicio de Nefrología, Hospital Clinico de Salamanca, Spain.* We evaluated the possible beneficial effect of the use of OKT3 McAbs on cadaver kidney transplantation. Over a 2-year period, we studied 68 patients receiving kidney grafts: two groups of 34 patients. One kidney from each patient was assigned to a group. In one group, patients received 5 mg/day OKT3 intravenously for four days before transplantation and on the day of transplantation, before the procedure (total of 5 days). They received steroids beginning at transplantation and cyclosporine A beginning 72 hours afterwards. In the second group, patients received cyclosporine A and steroids beginning at transplantation. In both groups, cyclosporine A and steroids were administered according to the same protocol. Both groups were similar with regard to age, male/female ratio, time on hemodialysis, hot and cold ischemia time and HLA incompatibility. We evaluated in both groups the incidence of acute rejection, steroid-resistant rejection, acute tubular necrosis, graft survival and serum creatinine levels. Results were:

	OKT23	Cyclosporine A	P
Acute Tubular Necrosis (X ± SD)[a]	0.35 ± 0.43	0.44 ± 0.50	NS[b]
Acute rejection (X ± SD)[a]	0.41 ± 0.65	0.55 ± 0.74	NS[b]
Steroid-resistant rejection (X ± SD)[a]	0.05 ± 0.23	0.08 ± 0.28	NS[b]
Graft Survival (18 months)	88.89%	88.46%	NS[b]

[a] X = median; [b] NS = no significant difference

In conclusion, the group of patients receiving OKT3 had a lower incidence of acute and steroid-resistant rejection and fewer of these patients had tubular necrosis. Serum creatinine levels were less altered in the OKT3-treated group, but the difference was not significant. At 2 years post-transplant, graft survival was similar in both groups.

Renal transplantation: Induction immunosuppressive regimen with ALG. Ten years of experience. *F.J. Paúl Ramos, R. Moreno, M.P. Martínez, C. González, A. Garbayo, L. Pastor, J. Pérez, A. Sanjuán, L. Marzo, C. Buñuel, J.A. Gutiérrez Colón, Nephrology and Hematology Departments, Hospital "Miguel Servet," Zaragoza, Spain.* Renal transplantation (RT) has become the most suitable therapeutical alternative for a great number of patients undergoing dialysis treatment. A better knowledge of the immune response, a well established surgical technique, a better control of immediate post-transplant period and management of infectious complications and the development of new immunosuppressive drugs that are more potent and selective have led to an important increase in patient and graft survival rates. The kidney transplantation program started in our Hospital in June 1986; 330 cadaver transplants have been done until March 1996. Mean age for donors was 36.5 ± 16.5 years (1–74); 66.8% were male and 33.2% females. Death related to craneoencephalic traumatisms occurred in 60.1% of donations vs. 31.9% due to hemorragic brain events. Mean cold ischemia time was 18.1 ± 4.3 hours (5.6 to 31.7). Recipient's mean age was 47.5 ± 13.5 years (17 to 71); 69.4% were male vs. 30.6% females. Patients' mean time of stay under hemodialysis treatment was 44.8 ± 36.4 months (2 to 216). Glomerular disease was the most common cause of ESRD (39.7%) vs. 25.8% related to interstitial diseases; 13.4% of recipients had polycystic kidney disease. All patients received cyclosporine from the first day post-transplantation. A total of 234 patients (70.9%) were included in an inductive immunosuppressive protocol with polyclonal antilymphocyte globulin (ALG) (10 mg/kg/day, 3–6 doses) in the immediate post-transplant period. The overall survival rate for patients and grafts was 93.0% vs. 89.0 at 1 year, 91.9% vs. 86.2% at 3 years, 84.7% vs. 76.9% at 6 years, and 81.3% vs. 71.1% at 9 years. The incidence of acute tubular necrosis (ATN) (18.1%), acute rejection epidodes (31.8%) and complications associated to immunosupression with ALG will be evaluated in this study. The use of an induction protocol with ALG in our kidney transplanted patients has shown an excellent graft and patient short-term and long-term survival rate, reduced incidence of ATN and acute rejection episodes, and a low rate of complications associated with immunosuppression.

Perioperative changes in coagulation and in fibrinolysis; role of different immunosuppressors. *J. Deira, J.L. Lerna, B. Martín, I. Alberca, A. Gascón, J.M. Tabernero, Servicio de Nefrología y Hematología, Hospital Clínco de Salamanca, Spain.* To evaluate the effect of cyclosporine A and of OKT3 McAbs on renal vessel thrombosis immediately after kidney transplantation, we studied 19 transplant recipients. Ten patients (Group A) received 5 mg/kg/day of OKT3 and prednisone for the first five days after transplant. Nine patients (Group B) received cyclosporine hours before transplantation and in the post-transplant period at doses sufficient to maintain therapeutic levels as well as prednisone at doses similar to those given to patients in Group A. One kidney from each donor was assigned to a group. Blood samples were collected before the surgical procedure and at 2, 4, and 24 hours after the induction of anesthesia; samples were immediately stored at −20°C. There were no differences between groups with regard to age, time on hemodialysis, hemoglobin, platelets, the usual coagulation parameters, hepatic function, HLA compatibility, or cold ischemia. In both groups, the following were measured: 1) coagulation activation markers—prekalikrein (PKK) and thrombin-antithrombin complexes (TAT); 2) markers of endothelial damage—thrombomodulin (TMD) and plasminogen tissue activator (tpA); 3) suppressors or inhibitors of hemostasis—antithrombin III (AT-III) and protein C (PC); and 4) markers of fibrinolysis—plasminogen (PGL) and α-2 antiplasmin (α2APL). In both groups (see Table), there was a significant activation of coagulation (PKK consumption and TAT formation) and fibrinolysis (decrease in PLG and α2APL), and a decrease in inhibitors of hemostasis (AT-III and PC). These findings suggest that the hypercoagulation state and subsequent fibrinolysis may be the result of surgery. Patients receiving OKT3 had increased tpA levels at 2, 4, and 24 hours as compared to the group receiving cyclosporine A ($P < 0.0001$), with no differences in TMD between the groups—pointing to a slight degree of endothelial damage. In conclusion, we found that coagulation is activated 2 hours after transplantation and persists for at least 24 hours. Also, the fall in AT-III and PC levels could be responsible for the risk of thrombosis in kidney transplantation, regardless of the immunosuppressor used.

	PKK	TAT	PLG	α2APL
		OKT3		
Basal	94 ± 8	9 ± 2	98 ± 9	102 ± 5
2 hours	84 ± 7	28 ± 6	79 ± 4	92 ± 8
4 hours	88 ± 9	34 ± 7	77 ± 7	83 ± 5
24 hours	66 ± 9	20 ± 3	59 ± 4	79 ± 5
	AT-III	PC	tpA	TMD
Basal	95 ± 6	124 ± 9	5 ± 1	270 ± 29
2 hours	78 ± 5	97 ± 7	26 ± 3	224 ± 31
4 hours	70 ± 9	91 ± 8	29 ± 3	219 ± 32
24 hours	52 ± 6	63 ± 7	15 ± 1	184 ± 25
		Cyclosporine A		
Basal	87 ± 6	8 ± 1	89 ± 3	101 ± 2
2 hours	76 ± 5	13 ± 4	77 ± 4	89 ± 2
4 hours	78 ± 6	20 ± 3	75 ± 4	89 ± 4
24 hours	56 ± 4	22 ± 4	63 ± 3	81 ± 3
Basal	93 ± 4	121 ± 9	4 ± 1	328 ± 22
2 hours	82 ± 5	101 ± 8	7 ± 2	242 ± 29
4 hours	76 ± 5	91 ± 8	10 ± 3	227 ± 23
24 hours	65 ± 5	73 ± 6	7 ± 2	194 ± 20

Effect of the new HMGCoA reductase inhibitor fluvastatin on the treatment of hypercholesterolemia after renal transplantation and with cyclosporine immunosuppression; preliminary results. *A.M. Castelao, J.M. Griñó, C. Fiol, M.J. Castiñeiras, I. Hurtado, S. GilVernet, D. Serón, I. Porta, A. Miñarro, A. Villarroya, and J. Alsina, Hospital Princeps d'Espanya. C.S.U. Bellvitge, University of Barcelona, Spain.* We conducted a pilot study to investigate the effect of Fluvastatin (Fluv) on renal transplant recipients with persistent hypercholesterolemia (above 6.5 mmol/liter) after 3 months of dietary lipid restriction. We treated 20 patients (12 males and 8 females, mean age 46 ± 10 years) with Fluv, 20 mg/day, along with cyclosporine A and prednisone, for 12 weeks. After that time period, the 9 patients with hypercholesterolemia greater than 6.3 mmol/liter were given 40 mg/day Fluv (Group I); the 10 patients with hypercholesterolemia less than 6.3 mmol/liter (Group II) continued to receive 20 mg/day Fluv. One patient developed nausea and vomiting after three weeks and was excluded from the study. Biochemical and lipid measurements in blood were:

	Group I		Group II	
	Before treatment	After 12 months treatment	Before treatment	After 12 months treatment
Creatinine *μmol/liter*	134 ± 43[a]	161 ± 64	175 ± 41	176 ± 52
Proteinuria *g/day*	0.35 ± 0.27	0.64 ± 0.8	0.48 ± 0.5	0.6 ± 0.6
Total cholesterol *mmol/liter*	7.2 ± 0.5	5.66 ± 0.7[a]	8.2 ± 0.7	6.7 ± 0.6[a]

	Group I		Group II	
	Before treatment	After 12 months treatment	Before treatment	After 12 months treatment
Triglycerides *mmol/liter*	2.8 ± 0.8	1.66 ± 0.9	2.6 ± 1.8	3 ± 1.5
HDL *mmol/liter*	1.6 ± 0.4	1.42 ± 0.4	1.2 ± 0.4	1.2 ± 0.3
LDL *mmol/liter*	5.1 ± 0.5	3.64 ± 0.6[a]	5.9 ± 0.6	4.3 ± 0.4[a]
VLDL *mmol/liter*	0.5 ± 0.4	0.59 ± 0.2	0.9 ± 0.4	1.1 ± 0.6
Apo A1 *g/liter*	1.6 ± 0.6	1.54 ± 0.4	1.6 ± 0.2	1.1 ± 0.6[a]
Apo B *g/liter*	1.4 ± 0.1	1 ± 0.03	1.5 ± 0.1	1.3 ± 0.3

[a] $P < 0.05$

There were no significant increases in ALT, AST or CPK. Plasma levels of cyclosporine A increased significantly in week 13 of the study (from 196 ± 50 to 229 ± 49 nmol/liter, $P = 0.05$), but decreased thereafter. After 12 months of treatment, total cholesterol had decreased 21.3% in group I and 18% in group II. In conclusion, Fluv significantly reduced total cholesterol and LDL cholesterol levels, with no severe side effects.

Induction of immunosuppression with antilymphocyte globulin after renal transplantation; ten years of experience. *F.J. Paúl Ramos, R. Moreno, M.P. Martínez, C. González, A. Garbayo, L. Pastor, J. Pérez, A. Sanjuán, L. Marzo, C. Buñuel, and J.A. Gutiérrez Colón, Nephrology and Hematology Departments, Hospital "Miguel Servet," Zaragoza, Spain.* Renal transplantation (RT) has become the most suitable therapeutic alternative for patients undergoing dialysis. Increased graft and patient survival rates have developed as a consequence of greater knowledge of the immune response, experience with surgical technique, better medical control of the immediate post-transplant course, and the advent of more potent and more selective immunosuppressive drugs. From June, 1986, when our transplant program began, to March, 1996, 330 cadaver kidney transplants were performed in our hospital. The mean age of donors was 36.5 ± 16.5 years (range, 1–74 years); 66.8% were males and 33.2% females. Death related to cranioencephalic trauma occurred in 60.1% of donors; death related to brain hemorrhage occurred in 31.9%. The mean cold ischemia time was 18.1 ± 4.3 hours (range, 5.6–31.7 hours). The mean age of recipients was 47.5 ± 13.5 years (range, 17–71 years); 69.4% were male and 30.6% female. Mean length of time on dialysis was 44.8 ± 36.4 months (range, 2–216 months). Glomerular disease, occurring in 39.7% of kidney transplant recipients, was the most common cause of end-stage renal disease in these patients, followed by interstitial diseases (25.8%) and polycystic kidney disease (13.4%). All patients received cyclosporine from the first day post-transplantation. In the immediate post-transplant period, 234 patients (70.9%) were given polyclonal antilymphocyte globulin (ALG), 10 mg/kg/day, 3–6 doses, to induce immunosuppression. Overall survival rate for patients and grafts was 93.0% vs. 89.0% at 1 year post-transplant; 91.9% vs. 86.2% at 3 years post-transplant, 84.7% vs. 76.9% at 6 years post-transplant, and 81.3% vs. 71.1% at 9 years post-transplant. The incidence of acute tubular necrosis was 18.1% and the incidence of acute rejection was 31.8% in the ALG-treated group. In conclusion, the use of ALG to induce immunosuppression has been associated with excellent graft and patient short-term and long-term survival, a reduced incidence of acute tubular necrosis and acute rejection episodes, and a low rate of immunosuppression-related complications.

Predictive value of BANFF criteria in acute rejection of kidney transplant. Comparison with immunohistochemical quantification of glomerulointerstitial infiltrate. *A. Osuna, C. Ramírez, R. Esteban, F. O'Valle, J. Osorio, M. Gómez-Morales, C. Asensio, R. Carvia, and R.G. Del Moral, Department of Pathology, University Hospital, Nephrology Service, Virgen de las Nieves Hospital, Granada, Spain.* The progressive introduction of the BANFF criteria for the diagnosis of acute kidney transplant rejection has facilitated the unification of pathological criteria that define rejection, and has made it easier to reach a decision regarding appropriate treatment. However, problems remain with the interpretation of these criteria, and their predictive value regarding the future functioning of the transplanted organ has yet to be determined. We present a comparative study of the BANFF criteria and more traditional systems based on histological classification (vascular, interstitial and severe glomerulointerstitial rejection) and on counts per mm^2 of inflammatory glomerulointerstitial infiltrates. We studied 42 biopsies from patients with acute kidney transplant dysfunction. None of the patients had received prior treatment, and all were diagnosed histopathologically on the basis of conventional criteria. These biopsies were subsequently studied according to BANFF criteria by two independent observers. When the results between the two observers were discrepant, they were agreed on by consensus. Frozen sections of the biopsy material were prepared for standard counts of glomeruli and interstitial leukocyte subpopulations, using mAbs that recognized CD45, CD3, CD4, CD8, CD16, CD20, CD57 and CD68. Reclassification on the basis of BANFF criteria revealed a high proportion of borderline rejections (28.6%) in comparison with 7% borderline cases found with counts of inflammatory infiltrating cells in the renal interstitium. Deterioration of renal functioning, measured as serum creatinine level at the end of clinical treatment, was not related with the classification obtained with BANFF criteria, or with interstitial counts of infiltrating leukocytes in the transplanted organ. In contrast, final serum creatinine levels were strongly associated with glomerular infiltration determined with CD3 ($r = 0.50$, $P < 0.01$), CD8 ($r = 0.41$, $P < 0.05$) and NK cells ($r = 0.71$, $P < 0.001$). In conclusion, (1) although the BANFF criteria facilitate the classification of moderate and severe acute rejection reactions, they do not firmly distinguish between slight or borderline rejection and other causes of acute transplant dysfunction. (2) The presence of severe glomerulitis (CD8+ T cells and NK cells) is of greater value than the BANFF criteria in predicting progression toward renal insufficiency.

P-glycoprotein expression in peripheral blood lymphocytes in kidney transplant patients. Relationship with acute rejection. *F. O'Valle, A. Osuna, F. Arrebola, G. Alvarez, M. Guillen, T. Martínez, C. Asensio, and R.G. Del Moral, Dept. of Pathology, University Hospital, Nephrology Service, Virgen de las Nieves Hospital, Granada, 18012, Spain.* P-170 glycoprotein (P-gp) is a detoxicant system related with multidrug resistance (MDR) in some tumors. The protein removes hydrophobic substances such as chemotherapeutic and immunosuppressive agents, including cyclosporine A (CsA), from the cell. Transplant patients who develop rejection refractory to treatment have high levels of mRNA for P-pg in circulating lymphocytes. We tested the hypothesis that CsA induces overexpression of P-gp in lymphocytes in transplant patients, and this may condition the appearance of acute rejection and the response to treatment with steroids. We studied 123 patients: 105 with kidney transplant, treated with CsA; 18 on hemodialysis; and 15 healthy controls. Acute rejection was treated with a bolus of steroids, and if resistance was found, with monoclonal antibody OKT3. In all patients we assessed clinical and laboratory findings, and took blood samples to monitor P-gp with flow cytometry and indirect immunocytochemistry using mAb JSB1, which recognizes an intracytoplasmic epitope of P-gp. Statistically significant differences were found between the percentage of lymphocytes that expressed P-gp in transplant patients (32 ± 18), patients on hemodialysis (20.4 ± 14), and healthy controls (8.9 ± 4.2) (Anova, $P < 0.05$). The number of P-gp molecules per cell was also increased (17.8 ± 8 vs 13.1 ± 11, $P < 0.1$). In patients with acute transplant rejection, the mean percent expression of P-gp was 47.9 ± 18%, vs 29.25 ± 17% in transplant patients without rejection ($P < 0.05$). P-gp expression was highest in patients with acute rejection resistant to steroids (52.4 ± 25, vs 45.9.9 ± 16 in patients with nonresistant rejection), although the difference did not reach significance. In conclusion, P-gp is elevated in kidney transplant patients treated with CsA, and this increase is related to acute rejection. Measurement of P-gp in peripheral blood can be of use in predicting acute rejection, and in detecting resistance to treatment.

Pneumonia in patients with renal allograft. *A. Solís, J.J. Amenabar, I. Gimeno, L.M. Ruiz-Muñoz, P. Gomez-Ullate, I. Lampreabe, and L.A. Ruiz, Nephrology Department, Cruces Hospital, Baracaldo, Basque Country, Spain.* We wanted to study the incidence, clinical and microbiological findings of the pneumonic episodes detected in our transplanted population. Pneumoniae registered in our renal transplantation program between 1-1-85 and 31-12-95 have been included. Pneumonia was defined as an inflammation of the pulmonary parenchyma with clinic and thorax RX compatible. A total of 89 pneumonic processes were found among in 807 transplant recipients. They were 59 males and 30 females with an average age of 47 (range 15–73). The average post-transplant time was 592 ± 841. Seventeen patients were receiving azathioprine and prednisone (19.3%), 33 cyclosporine and prednisone (37.5%), 37 triple therapy (41.5%), and 30

patients had been treated in one occasion with methylprednisolone as antirejection therapy (34%). Ten were treated more than once (11%) and 3 with Ac OKT3 (3.3%). The pneumonic episode was bilateral in 35 patients (47.3%). There was moderate-severe hypoxemia ($pO_2 < 60$) in 13 (14.6%) and venial ($pO_2 < 70$) in 31 (34.8%). Nine required intubation. Bronchoalveolar lavage was practiced in 39 patients (48%) and found positive in 28 (72%). Positive hemocultures were in 26 (31.3%) and positive sputum cultures in 13 (16.2%). The final microbiological diagnostic in 48 of 89 (55.2%) found the following microorganisms: 17 CMV (19%), 10 M. tuberculosis (11.2%), 8 *P. Carinii* (9%), 7 Aspergillus (8%), 3 Pseudomonas, 2 Nocardias, 2 Salmonellas, 2 *S. pneumoniae* and 9 others (10%). In 6 of 8 cases CMV and *P. Carinii* coincided; in 3 of 10 CMV and M. tuberculosis and in 3/7 CMV and Aspergillus were together. Treatment wasn't introduced before the diagnostic attempt in 15 (17%); in 35 (39%) the initial treatment wasn't modified, and in 29 patients (32.5%) it was modified. The outcome in 66 cases was to recovery (74%) and in 23 to decease (26%); in 6 episodes the responsible agent was CMV, in 4 M. tuberculosis, in 3 *P. Carinii* and in 3 Aspergillus. The average hospital stay was 26.97 ± 19.75. Pneumonia is an important pathology among transplanted patients, due to both incidence and severity. Among the etiologies CMV, *P. Carinii*, M. tuberculosis and Aspergillus stand out. Polymicrobial infections are frequent and severe, being especially outstanding with regards to CMV.

Clinical characteristics in cyclosporine-treated and non-cyclosporine-treated adult renal cadaveric allograft recipients. *I. Lampreabe, J.J. Amenabar and the Spanish Transplant Cooperative Group, Nephrology Department, Cruces Hospital, Basque Country, Spain.* We investigated the clinical transcendence of the novo cancer, in adult patients who received renal cadaveric grafts, in relation to different immunosuppressive protocols. This retrospective study was performed in 6292 Spanish adult renal cadaveric allograft recipients. We included 2398 (38%) treated with azathioprine-prednisone (CIT group) and 3985 (62%) receiving cyclosporine (CsA group) as part of monotherapy (CsA), double (CsA + Pr), triple (CsA + Pr + Aza) or quadruple-therapy (CsA + Pr + AZA + ALG/ATG) protocols. Both groups were followed for 6 years. The number of patients at risk in each annual post-transplant interval and the total patient-year at risk were calculated. The cancer incidence in renal transplant patients, using the patient-year method and the actuarial survival, was estimated according to the log-rank test. Overall, 113 patients (2.8%) in the CsA group and 71 patients (3%) in the CTI group developed cancers. The malignancies were located in the CIT group and CsA group, respectively: skin and lip cancers 46% and 45%, Kaposi sarcoma 5.6% and 11.4%, lymphoma 7% and 15%, and uterine cancer 2.8% and 6.2%. The prevalence of skin cancers in transplant recipients was higher than the same variant of cancer prevalence in general population. Furthermore, CsA treated patients had a higher incidence of basal cell carcinoma, than non-CsA group ($P < 0.005$). The squamous cell carcinoma/basal cell ratio varied dramatically from 1.38 in the CIT group to 0.4 in the CsA group. The diagnostic interval in lymphoma, squamous cell carcinoma and basal cell carcinoma was shorter in the CsA group. In the actuarial analysis, the accumulative risk in CsA group to develop skin malignancy and non-skin malignancy, after 6 years, were 41 and 33 per 1000, respectively ($P < 0.001$). However, in the CIT group they were 12 and 20 per 1000, respectively. The cummulative risk to develop basocellular carcinoma cell, after six years, was 33 per 1000 in the CsA double therapy group, 10 per 1000 in the CsA triple therapy group, and 4 per 1000 in the CIT group. In the short-term, in immunosuppressive theraphy, there is a contrast between the benefit and the risk of cancer. The incidence of skin cancer and, especially basocellular carcinoma cell, increased in therapy with CsA.

Malignancies after renal transplantation. Comparative patterns with the general population. *G. Fernández-Juárez, J. Pascual, L. Orofino, F.J. Burgos, V. Gómez, T. Cano, A. Tato, F. Liaño, and J. Ortuño, Servicios de Nefrología y Urología, Hospital Ramón y Cajal, Madrid, Spain.* Malignant neoplasia is a major cause of morbidity and mortality in the renal allograft recipient. The epidemiologic patterns seem to be quite different in these patients (pt) than in the general population. Between 1979 and 1995, 609 renal transplants (RT, 595 cad, 14 liv) in 559 pt (393 males) were performed in our Unit. Basal immunosuppression was azathioprine and steroids (Aza-P $N = 205$) or cyclosporine A and steroids (CsA-P $N = 404$). Poly- or monoclonal antibodies were not used. Thirty malignant tumors were diagnosed in 29 (5%) pt (84% male). The age at RT was 56.3 ± 8 years and the age at the diagnosis was 60.7 ± 9 years (mean time before neoplasia 4.4 years post-RT, similar with Aza-P and CsA-P). The tumors were: cutaneous carcinoma ($N = 15$), Kaposi ($N = 3$), cutaneous T-lymphoma ($N = 2$), pulmonary epid carcinoma ($N = 3$), adenoca ($N = 5$) (2 native kidneys, 1 colon, 1 gastric, 1 prostatic), melanoma ($N = 1$) and astrocytoma ($N = 1$). The occurrence of malignant tumors was similar with Aza-P ($N = 14$) and CsA-P ($N = 16$) (NS); the 3 lung tumors were found in a Aza-P pt, and the 2 T-lymphomas in the CsA-P pt. We compared observed cases (O), expected cases (E: years at risk X known annual incidence in general population), and the O/E ratio:

	Lung	Gastric	Colon	Lymphoma	Prostatic
O	3	1	1	2	1
E	0.95	0.6	0.67	0.24	0.78
O/E	3.13	1.65	1.47	8.02	1.26

Mortality with tumor was 35% (13% with cutaneous neoplasia, 100% adenoca). The risk of suffering from any malignant neoplasia after RT was multiplied by 86. The risk of lung neoplasia triplicated that of general population and the risk of cutaneous lymphoma was multiplied by 8. No cases of postRT B cell lymphoproliferative disease were observed (no antibodies used!). The absence of breast or cervix cancer, frequent in healthy females is noteworthy. The use of CsA-P since 1986 does not represent any significant modifications in the patterns of cancer in our RT recipients.

Influence of blood pressure and antihypertensive drugs on Doppler spectrum analysis of the renal allograft. *L. Sánchez, J. Pascual, F.J. Burgos, L. Orofino, V. Gómez, G. Fernández-Juárez, A. Tato, T. Cano, F. Liaño, and J. Ortuño, Servicios de Nefrología y Urología, Hospital Ramón y Cajal, Madrid, Spain.* The prevalence of hypertension (HT) in the renal transplant population is very high, and its importance as a risk factor for graft dysfunction and patient survival is unquestionable. Doppler spectrum analysis has been used mainly to detect renal artery stenosis, but general patterns of blood flow and the influence of different antihypertensive drugs on them have been less frequently assessed. During two years, 232 renal allograft patients underwent such an analysis: 111 were normotensive (Group I), 92 had well-controlled HT (II) and 29 poorly-controlled HT (III) at the time of the study. Acceleration (AC), mean velocity (MV), peak systolic velocity (PSV) and minimal diastolic velocity (MnDV), as well as pulsatility (PI) and resistance index (RI) were measured in the external iliac, main renal, segmental, interlobar and arcuate allograft arteries. Patients from Group III had higher RI in the external iliac (ANOVA $P < 0.01$) and arcuata arteries, higher PI in the external iliac and lower PSV in the segmental and interlobar arteries (all $P < 0.05$). Patients taking nifedipine ($N = 62$) had lower PSV in the interlobar arteries than the remainder (24.3 ± 1.3 vs. 27.8 ± 0.9 cm/sec, $P < 0.05$). Patients taking beta blokers ($N = 49$) had lower MnDV in the external iliac (10.5 ± 1.2 vs. 13.5 ± 0.7 cm/sec, $P < 0.05$), higher MnDV in the segmental artery (9.5 ± 1.1 vs. 7.5 ± 0.4 cm/sec, $P < 0.05$), lower RI in the segmental artery (0.71 ± 0.02 vs. 0.76 ± 0.01, $P < 0.05$) and lower PI in the interlobar artery (1.46 ± 0.07 vs. 1.73 ± 0.06, $P < 0.05$). HT induces renal graft blood flow changes detectable by Doppler spectrum analysis. External iliac artery shows high RI and PI in hypertensive patients. Beta blokers reduce RI in large vessels and calcium antagonists lower RI and PI in small caliber intraparenchymatous vessels. Use of combinations of these drugs could be adequate for controlling renal transplant-associated HT. Doppler spectrum analysis might be useful in adjusting the most favorable combination.

Relationship between iliac artery histology and hemodynamic patterns in the renal allograft. *T. Cano, J. Pascual, F.J. Burgos, V. Gómez, L. Orofino, G.F. Juárez, F. Liaño, J. Ortuño, Servicios de Nefrología y Urología, Hospital Ramón y Cajal, Madrid, Spain.* Correct assessment of aortoiliac atheromatosis prior to kidney transplantation (KT) is essential. Doppler ultrasound (DU) is a noninvasive technique that provides an accurate hemodynamic study of the iliac and limb arteries, but the correlation of the findings with real histology is unknown. Seventy KT recipients were studied with DU immediately before KT. Acceleration (AC), mean (MV), maximal systolic (MxSV), minimal diastolic (MnDV) velocities (in cm/sec), and pulsatility (PI) and resistance (RI) indices were measured. We

performed an arterial biopsy during the KT surgical procedure in 26 of them, and a histological study was made. Total arterial thickening was 1150 ± 48 μ (intima 92 ± 43, medium 626 ± 21 and adventitia 430 ± 31). In 19% of the patients atherosclerotic plaques were observed, 4% of them with calcification. No relationship was found between arterial thickness and DU parameters. Several significant differences were found in DU parameters between arteries with and without atheromatosis (means ± SD):

	AC	MV	MxSV
No atheroma	757 ± 122	13 ± 2	62 ± 9
Atheroma	592 ± 101	6 ± 1	50 ± 7
P	<0.01	<0.05	<0.05

	MnDV	PI	RI
No atheroma	21 ± 2	7 ± 2	1.38
Atheroma	19 ± 1	6 ± 1	1.43
P	NS	NS	0.1

AC, MV and MxSV are lower in iliac arteries from KT with atherosclerosis. Illfemoral DU is a useful tool in the evaluation of atheromatosis and its severity in the KT recipient, and could be used in follow-up assessment and interventional studies.

Treatment of cyclosporine-induced gingival hyperplasia with azithromicyn in renal transplant patients. *I. Beneyto, J. Sanchez, I. Torregrosa, J. Garcia, J. Panadero, D. Ramos, A. Soldevila, A. Rochera, and J.M. Cruz, Nephrology Service, Hospital la Fe, Valencia, Spain.* Gingival hyperplasia is one important adverse effect of cyclosporine therapy that affects 30–70% of renal transplant patients. It appears to be worsened by the concomitant administration of nifedipine or phenytoin. Until now, we could only to advise patients of hygienic measures for oral cavity prevention, although the hyperplasia can appear in healthy mouths as well. Recently, however, have reported the utility of Azithromicyn in treatment of gingival hyperplasia. To verify the efficacy of this drug, we administered 500 mg on the first day and 250 mg over the next four days, to a group of fourteen patients (8 men and 6 women), aged 27 to 67 years, with gingival hyperplasia. Eight of these patients were treated simultaneously with nifedipine. We measured the levels of cyclosporine before and five days after treatment. All the patients improved after treatment, only one patient did not have any effect from the drug. At the beginning of therapy gingival bleeding after teeth brushing disappeared, and in next days the patients had less gingival erythema and retraction of the gums in various degrees. Blood levels of cyclosporine and creatinine did not show any significant change during treatment. The drug was well tolerated. Azitromicyn is an efficient treatment of cyclosporine-induced gingival hyperplasia, and is without adverse effects.

Risk factors predicting primary chronic dysfunction of renal allografts. *J.J. Amenábar, F. García-López, P. Gómez-Ullate, I. Minguela, M.I.. Muñiz, I. Lampreabe. Nephrology Service, Cruces Hospital, Baracaldo, Epidemiology Unit, Puerta de Hierro Hospital, Madrid, Spain.* The risk factors leading to the development of allograft chronic dysfunction are not fully understood. In this study we have included 197 from a total of 250 renal transplant recipients who participate, at our center, in a randomized trial comparing Double Therapy (CsA + Est) and Triple Therapy (CsA + Est + Aza). We excluded 53 patients who lost the allograft or had chronic renal dysfunction by causes other than chronic rejection. Patients were followed from 1 to 4 years. The slope (β) of 1/creatinine over time, analyzed by simple linear regression, was calculated in every patient. A diagnosis of chronic renal dysfunction was stated in patients with negative β, significantly different from zero ($P < 0.005$). Simple and multiple logistic regressions were performed using the following covariates: recipient and donor age and gender, primary cause of renal failure, time on dialysis, number of transplants, latest and highest PRA, HLA A-B-DR mismatches, initial graft function and cold ischemia time. The best multiple logistic regression model is shown in the table.

Variable	Coefficient	Odds ratio (95% CI)	*P*
Recipient age	−0.040	0.96 (0.93–1)	0.036
Female recipient	−1.147	0.32 (0.12–0.83)	0.015
Female donor	1.154	3.17 (1.29–7.76)	0.011
Transfusions ($N = 5$)[2]	0.001	1 (0.99–1)	0.06

The goodness fit of this model was high. Confounding and interaction tests were not significant. To linearize the number of transfusions (N) a square transformation was performed. The mean of transfusions received by patients was 5. The youngest patients, male recipients, female donors and both non-transfunded patients and those with many transfusions are associated with higher rate of chronic renal dysfunction.

Recurrent focal glomerulosclerosis (FGS) in the renal transplant. Apheresis therapies. *M.C. Vozmediano, F. Anaya, E. Verde, L. Inchaustegui, P. Rodriguez, M.L. Rodriguez, I. Lorenzo, F. Gómez, and F. Valderrabano, Nephrology Department, Hospital "Gregorio Marañón," Madrid, Spain.* FGS is the most important recurrent glomerulopathy in the renal transplant. Six patients (5 M; 1 F) with a histologic diagnosis of early recurrent FGS were studied. The mean age was 20 ± 10 years. Three patients were treated with apheresis therapies, plasmapheresis (PF) and inmunoadsorption (IADS), immediately after the onset of proteinuria. The first patient was treated with six sessions of PF. He had a remission of proteinuria and renal function has remained stable. The second patient, a 19-year-old girl who received a third transplant, had lost the previous grafts to recurrent FGS. She was treated with two courses of PF (10 sessions) with a partial reduction of proteinuria (mean total urine protein excretion before PF, 14 g/day; after PF, 3 g/day). A course of IADS (1 session/week) with phenylalanine was initiated during 50 days with no changes noted in proteinuria and renal function (serum creatinine 1.5 mg/dl). When apheresis treatment was discontinued creatinine clearance decreased significantly and hemodialysis therapy was required three months later. The third patient, a 20-year-old man who received a second transplant, was treated with IADS (6 sessions) rapidly after the onset of proteinuria. Subsequently he experienced a notorious decrease in proteinuria. His urine protein excretion and renal function has remained stable with a serum creatinine levels about 1.8 mg/dl, which are unchanged in last 5 months. Apheresis therapies were not used in three of the six patients. Proteinuria remitted spontaneously in one of them. Renal function deteriorated and long-term dialysis was required in the other two patients. In conclusion, recurrent FGS in renal transplant is a severe disease, usually leading to graft loss. FGS is generally unresponsive to conventional treatment. Our experience indicates that apheresis therapies could be effective in the treatment of recurrent FGS.

Effect of angiotensin converting enzyme inhibitors (ACEI) on the progressive graft failure and proteinuria in kidney transplant (KT) patients with chronic rejection. *D. Paredes, R. Sola, L. Guirado, J. Ibeas, I. Agraz, D. Vizcarra, F. Algaba, A. Oliver, Kidney Transplant Unit, Nephrology Service, Fundacion Puigvert, Barcelona, Spain; Department of Nephrology, Medical School, Universidad Nacional de Colombia, Bogota, Colombia; Section of Pathology and Service of Laboratories, Fundacion Puigvert, Puigvert, Spain.* Chronic rejection (CR) is a progressive graft failure (GF) appearing in some KT months or years after transplant, which is usually resistant to modifications in immunosupressive treatment. It could be due to immunologic and nonimmunologic mechanisms, such as a compensatory glomerular hyperfiltration (GHF) of the remanent nephrons, when multiple factors (ischemia, acute rejection, etc.) decrease an already reduced nephron population (single KT, suboptimal donors), such as in diabetic nephropathy (DN). A protective effect of some ACEI has been described in DN by decreasing this GHF. By analogy, we studied the effects of captopril and enalapril in patients with CR assuming that they have GHF. From patients with KT performed between January 1984 and December 1994, we selected 21 patients: 15 male and 6 female, ages ranging from 14 to 62 years. The chronic inmunosupression (CI) was respectively cyclosporine and prednisone (PDN), both in combination with azathioprine (AZA), or PDN with AZA in 13, 6 and 2 patients. When other treatable causes of GF have been ruled out, CR was suspected when a progressive proteinuria (Protu), a sustained increase in serum creatinine (Cr) or both, were present (5, 3 and 13 cases). A kidney biopsy (KB)

confirmed the diagnosis of CR (Banff classification). Eleven patients started captopril (25 mg/day) and 10 enalapril (5 mg/day), and continued indefinitely. The final doses were adjusted to blood pressure. If necessary, in the 17 previously hypertensive patients other antihypertensive therapies were modified. Clinical evaluation, Cr, 24 hour Protu, cyclosporine A levels, and other hematological and biochemical index were performed quarterly. The medium values of Cr, reciprocal of Cr (1/Cr) and Protu are shown in the Table, begining 9 months before ACEI started, until 2 years of follow-up. The follow-up was 1 year in all patients, 2 years in 14, and 3 years in 11 patients. For statistical analysis a MANOVA (SPSS) for repeated measures was used. Comparing the periods before and after ACEI, the tendency in the increase in Cr and the respective reduction in 1/Cr were stopped to remain stable. The sustained increase in Protu was reversed, especially in the first semester and remained stable too. The differences in both tendencies were statistically significant (Table). These results were independent of the ACEI used, the grade of CR, the antihypertensive therapy and the type of CI. No adverse effect was observed with AECI.

	−9m	−6m	−3m	AECI	+3m	+6m
Cr *μmol/liter*	156.4	165.1	171.4	187.6	192.1	194.2
1/Cr ($\times 10^{-3}$)	7.14	6.81	6.58	6.15	6.01	5.96
Protu *g/day*	0.75	1.34	1.85	2.84	2.22	1.32

	+9m	+12m	+24m	*P*
Cr *μmol/liter*	192.3	204.8	192.4	0.044
1/Cr ($\times 10^{-3}$)	6.09	5.89	6.19	0.012
Protu *g/day*	1.27	0.97	1.05	0.014

In our group of patients with CR, the patients use of an ACEI reduced the progressive GF and the degree of proteinuria significantly, and patients continued to be stable after two years of follow-up. Those effects could be due to the hemodynamic actions of the ACEI in decreasing a supposed already established GHF.

Natural killer cell subsets and coexpression of activated antigens in TCR$\alpha\beta$ and TCR$\gamma\delta$ T-lymphocytes in peripheral blood of patients with acute rejection of renal allograft. *A. Gascón, A. Orfao, J.L. Lerma, J. Ciudad, A. López, E. Iglesias, J.M. Tabernero, S. Nephrology and Cytometry, University. Hospital, Salamanca, Spain.* The allospecific cytotoxic immune response by T lymphocytes and/or NK-cells plays an important role in the pathogenesis of acute rejection of renal allograft (ARRA). The aim of the present study was to analyze the coexpression of the CD25 and HLA-DR activation-associated antigens in both the TCR$\alpha\beta$+/CD3+ and the TCR$\gamma\delta$+/CD3+ T-cells, and the distribution of different NK-cell subsets (CD3−CD16+CD56+, CD3-CD16+CD56−, CD3−CD16−CD56+) in peripheral blood (PB) of patients with histologically well-defined ARRA. A total of 11 patients and 18 healthy controls were studied. PB samples were analyzed by three-color flow cytometry analysis. Results expressed in absolute numbers and percentage of the total TCR$\alpha\beta$, and the total TCR$\gamma\delta$ and NK-cells in brackets are shown below.

	TCR$\alpha\beta$+	$\alpha\beta$+CD25+	$\alpha\beta$+DR+
CONT	1092	347 (32%)	153 (14%)
RA	605	343 (62%)	333 (55%)
t-test	$P < 0.01$		

	TCR$\gamma\delta$+	$\gamma\delta$+CD25+	$\gamma\delta$+DR+
CONT	68	18 (17%)	10 (14%)
RA	29	5 (11%)	19 (53%)
t-test	$P < 0.02$		

	NK Total	CD16+CD56+	CD16+CD56−	CD16−CD56+
CONT	351	301 (86%)	30 (8%)	20 (6%)
RA	150	69 (46%)	33 (20%)	59 (34%)
t-test	$P < 0.01$	$P < 0.001$		$P < 0.05$

In summary, our results show that there is an increased percentage of TCR$\alpha\beta$+ cells that coexpress the CD25 and HLA-DR activation associated antigens in patients with ARRA. Interestingly, the expression of HLA-DR on the $\gamma\delta$ T-cells, but not that of CD25, is also increased. These results indicate that different mechanisms may be involved on the activation of $\alpha\beta$ and $\gamma\delta$ T-cells in acute rejection of renal allograft. The ARRA induces a redistribution of the PB NK-cell subsets with a significant decrease of the mature CD3−CD16+CD56+ cells and a significant increase of the immature CD3−CD16−CD56+ NK-subset, suggesting that ARRA patients may have a decreased NK-cell cytotoxic activity.

Prednisone withdrawal more than five years after cadaveric renal transplant. *P. Gómez-Ullate, J.J. Amenabar, I. Minguela, M.L. Muñiz, M.P. Martinez, S. Zárraga, and I. Lampreabe, Servicio de Nefrología, Hospital de Cruces, Bilbao, Spain.* We evaluated the safety and clinical benefits of withdrawing prednisone (P) in 50 cadaveric renal transplant patients who had stable renal function for at least 5 years and who were receiving P and cyclosporine A (CsA) for immunosuppression. All patients had received a first cadaver transplant in the time period July 1980 to December, 1988. All patients were over the age of 15 years, and all had a serum creatinine (S_{Cr}) level less than 2 mg/dl, proteinuria less than 0.50 mg/min, and PRA less than 25%. None of the patients had experienced acute or chronic rejection of the transplanted kidney. All patients gave their written permission to be included in the study. We selected 25 patients at random to continue receiving both CsA and P, and 25 patients for the P-withdrawal group. There were no differences between the groups with regard to age, gender, B-DR mismatches, previous transfusions, immediate graft function, age of donor, or cold ischemia time. In the P-withdrawal group, doses of P were gradually tapered over a period of 3 months. There were no episodes of rejection in the control group. There was no graft loss or death in either group. Five patients in the P-withdrawal group (20%) who experienced acute rejection were treated with oral or intravenous 6-MP pulses and returned to the double therapy regimen. Clinical tolerance of P withdrawal was good in 18 of the 25 patients (72%), average in 3 (12%) and poor in 4 (16%). One patient could not tolerate the protocol and was withdrawn from study. None of the patients in either group exhibited a change in body weight. The incidence of hypertension was reduced from 64% to 52% in the P-withdrawal group and from 68% to 62% in the control group. In the P-withdrawal group, significant differences ($P < 0.01$) were documented between pre-withdrawal values and 2-year post-transplant values for: S_{Cr} (1.15 ± 0.26 to 1.25 ± 0.24), C_{Cr} (84.9 ± 28.55 to 74.28 ± 23.25), BUN (21.25 ± 5.56 to 24.7 ± 7.11), CsA dosage (2.95 ± 0.61 to 3.19 ± 0.66), total cholesterol (257 ± 35.56 to 241 ± 55.28), glucemia (82.16 ± 9.36 to 87.33 ± 9.1) and albumin (4.02 ± 0.19 to 4.2 ± 0.25). After one year, there were no differences in phospho-calcium metabolism or in bone densitometry results in either group. The prevalence of cataracts was decreased from 54% to 31% in the P-withdrawal group after one year and increased from 45% to 53% in the control group. There were no changes in dermatological effects. In conclusion, in 76% of the selected patients with graft survival exceeding 5 years, the withdrawal of P was possible and well tolerated. There was a 20% incidence of acute rejection but no graft loss. A discreet but non-progressive decline in renal function was found 2 years after P withdrawal. Some patients experienced clinical and metabolic improvements.

Effect of kidney transplantation (KT) and cyclosporine treatment on sexual performance and hormonal profiles in males with chronic renal failure. *J. Pascual, F.J. Burgos, V. Gómez, L. Orofino, T. Cano, A. Tato, G.F. Juárez, F. Liaño, and J. Ortuño, Servicios de Nefrología y Urología, Hospital Ramón y Cajal, Madrid, Spain.* Sexual dysfunction manifested by decreased libido and erectile failure is frequent in male ESRD patients. We have prospectively assessed the effect of KT on male sexual performance and hormonal profiles. Between 1991 and 1995, 50 male nondiabetic patients on dialysis were interviewed, evaluating libido, erection, ejaculation, orgasms and satisfaction. Plasmatic FSH, LH, testosterone

(TT), estradiol (ES) and prolactine (PRL) levels were measured. The mean age was 45.6 ± 5.9 years and duration of dialysis 15 ± 6 months. All of them received a cadaveric KT anastomosed to external iliac artery. A new questionnaire and hormonal profile were undertaken 16 ± 2 months post-KT. Blood pressure was similar pre- and post-KT, 60% needed drugs pre-KT and 80% post-KT. Nifedipine was more frequently used post-KT (20% vs. 80%, $P < 0.05$). Maintenance immunosuppression was cyclosporine (CsA) and prednisone (Pred) in 65%, azathioprine (AZA)-Pred in 7.5% and CsA-AZA-Pred in 27.5%. Complaints of reduced libido and reduced potency decreased after KT (40 vs. 30% and 60 vs. 45%, respectively, $P < 0.01$). FSH and LH levels were not different before and after KT and were directly correlated with time on dialysis. TT increased after KT (43.7 ± 22.3 vs. 298 ± 25.1 nM/liter, $P < 0.001$) and ES and PRL decreased (79.2 ± 12.9 vs. 28.4 ± 2.3 pmol/liter and 35.9 ± 8.7 vs. 11 ± 3.2, respectively, both $P < 0.05$). Antihypertensive type or doses did not influence the results. CsA-Pred treatment was associated with lower FSH and ES levels at any given level of graft function ($P < 0.05$ vs. the other regimens), and ES was inversely correlated with CsA dose. TT was directly correlated with hemoglobin and inversely correlated with S_{Cr} (both $P < 0.05$). KT improves libido and erectile function in some ESRD males, restoring a more adequate sexual hormonal profile (increases TT and reduces ES and PRL levels). CsA-Pred therapy seems to show more favorable effects than regimens with AZA. However, sexual dysfunction remains an important problem after KT.